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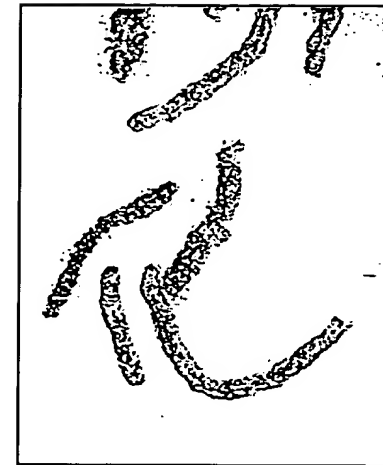
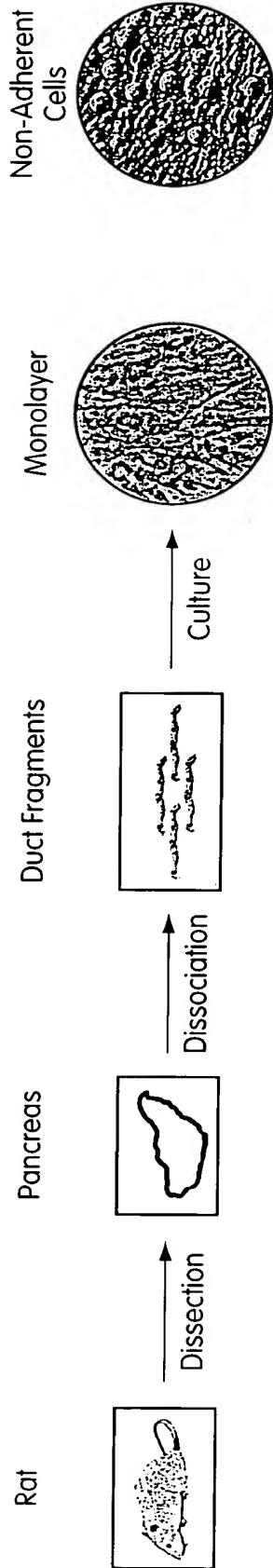
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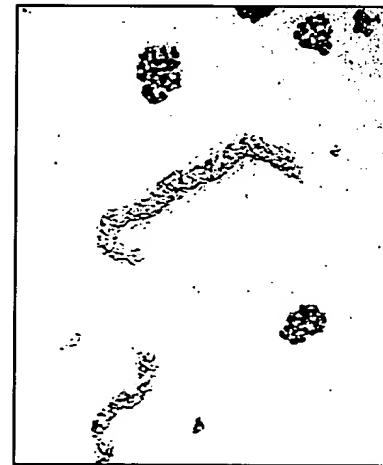
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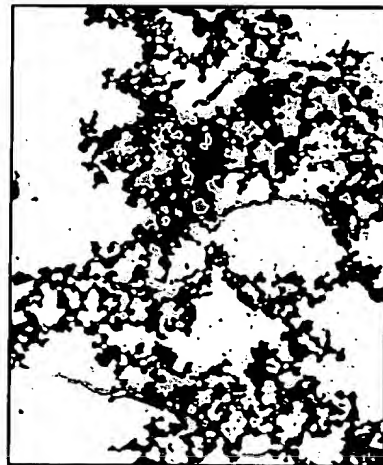
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Second Pick

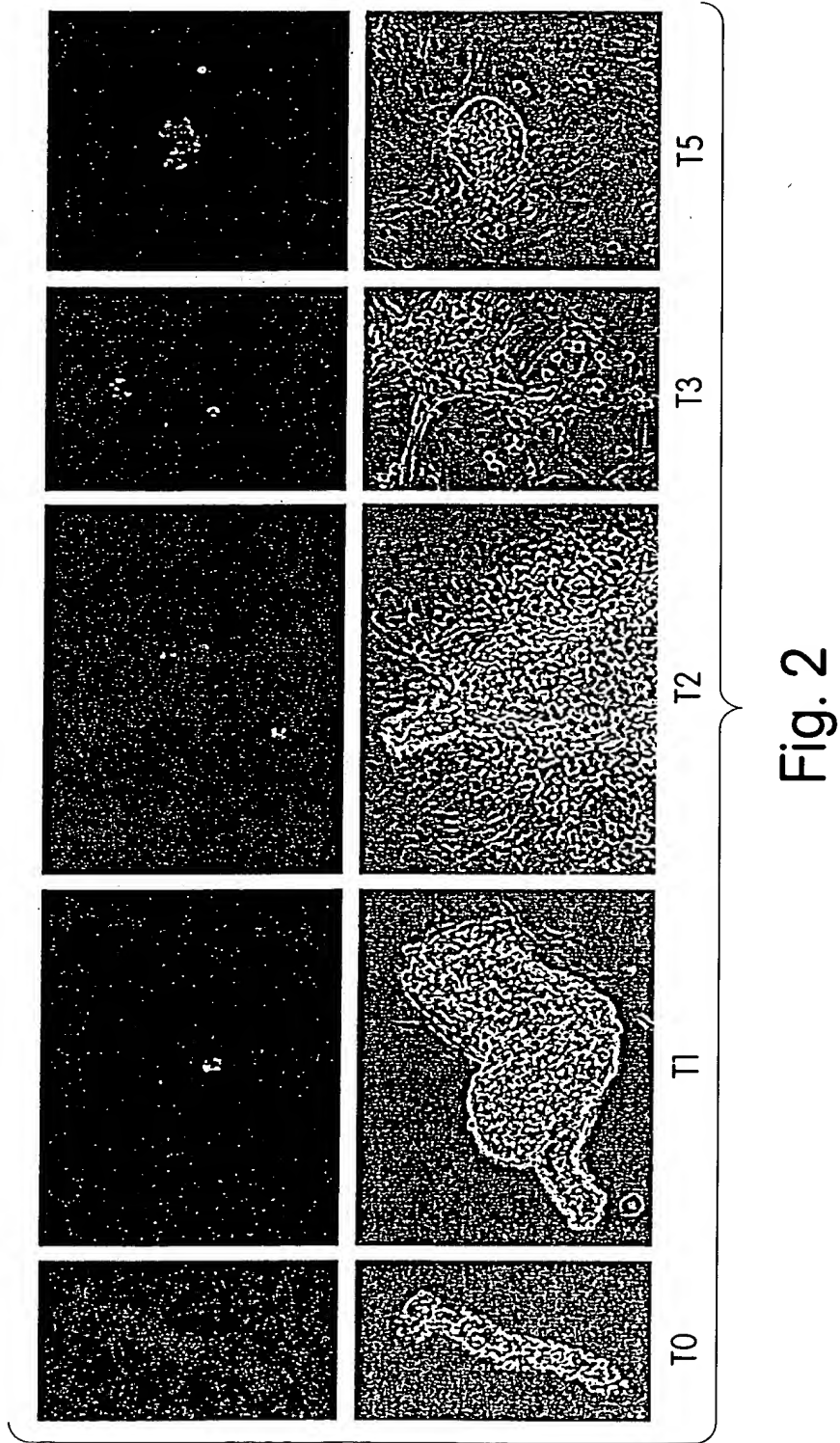


First Pick



Primary Digest

Fig. 1





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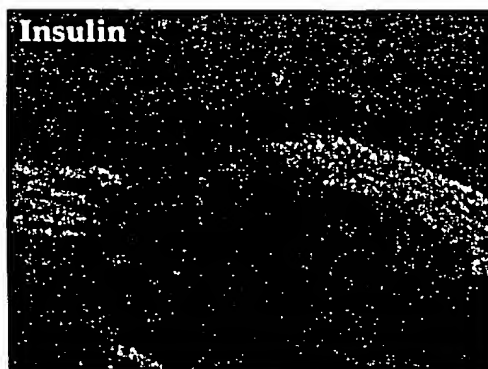


Fig. 3A

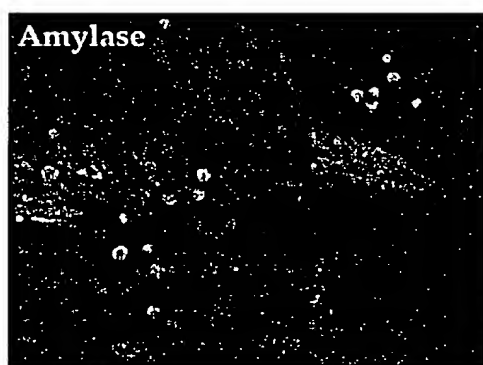


Fig. 3B

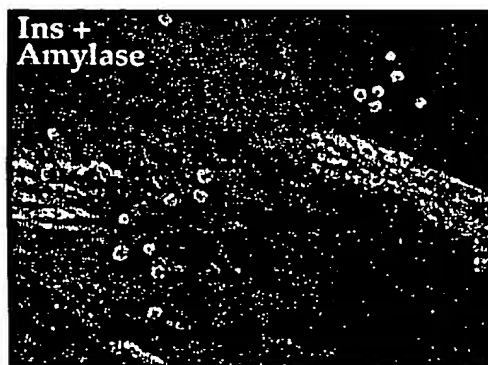


Fig. 3C



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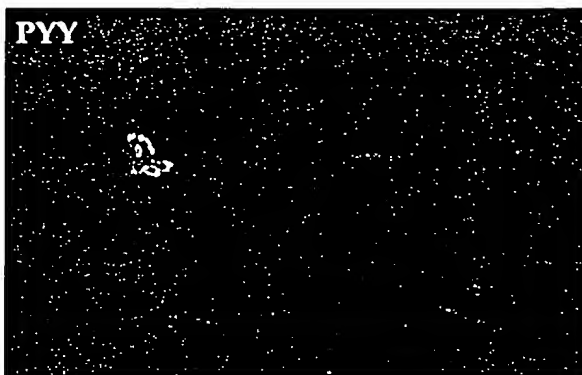


Fig. 3D

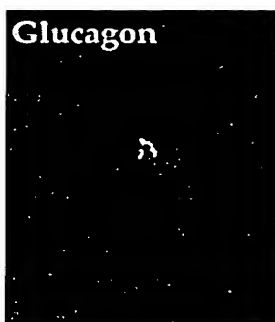


Fig. 3E

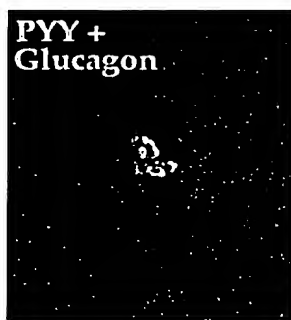


Fig. 3F

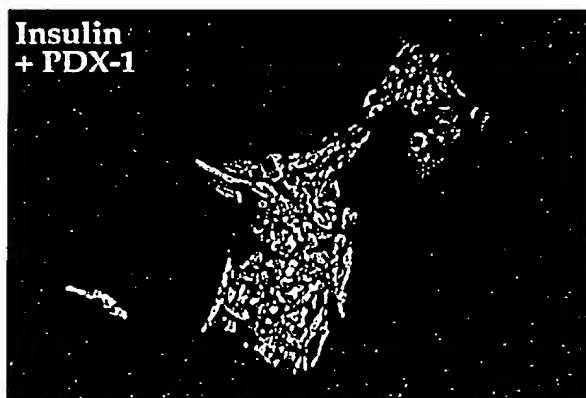


Fig. 3G



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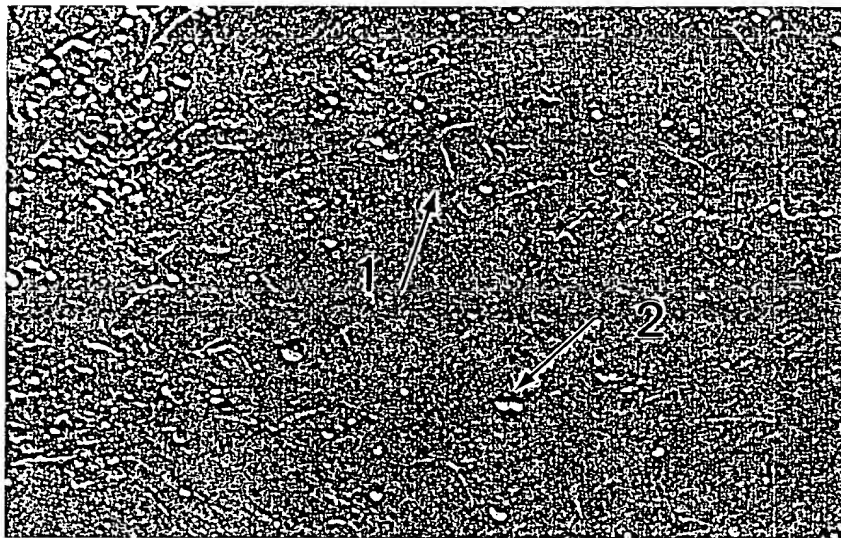


Fig. 4A

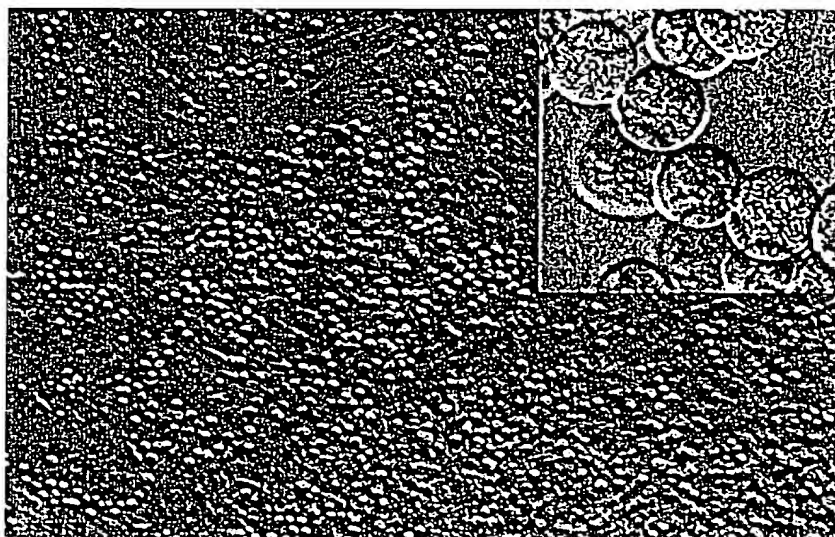


Fig. 4B



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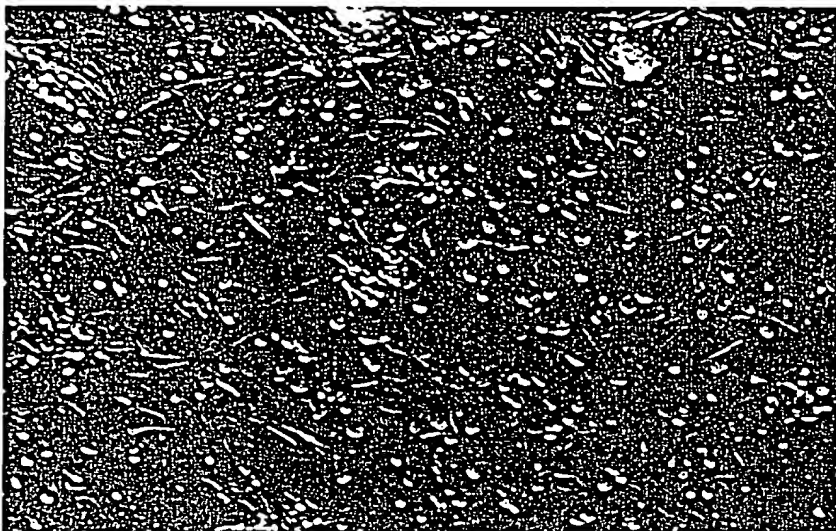


Fig. 4C

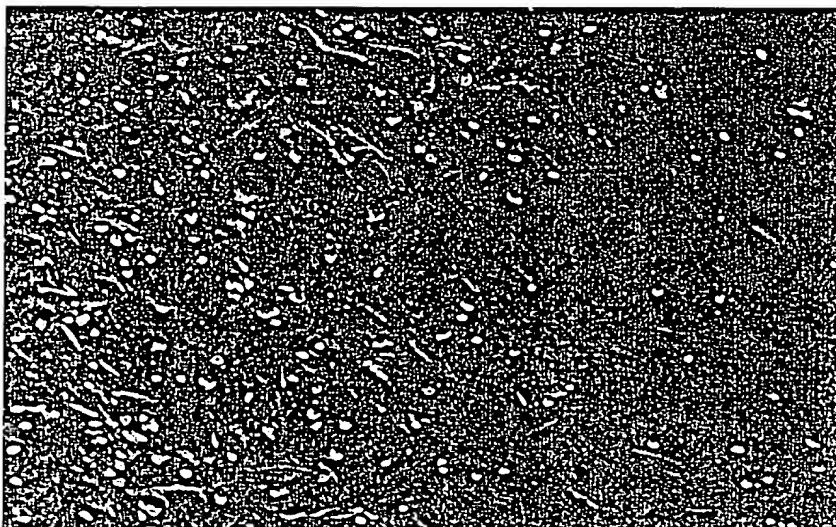


Fig. 4D



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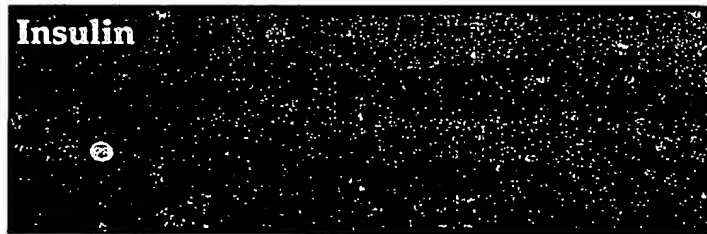


Fig. 5A



Fig. 5B



Fig. 5C





Fig. 5D



Fig. 5E



Fig. 5F

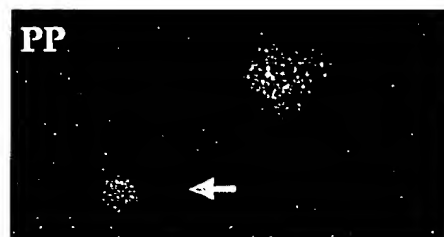


Fig. 5G

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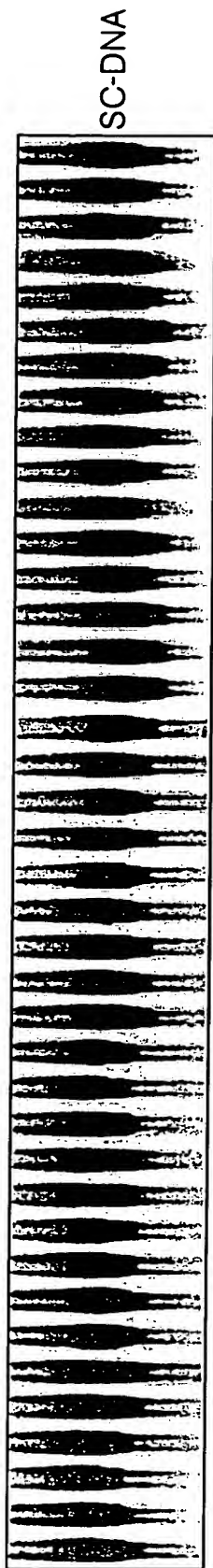


Fig. 6A

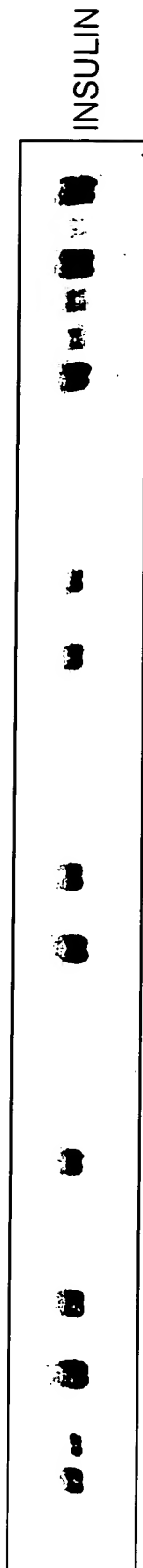


Fig. 6B



Fig. 6C

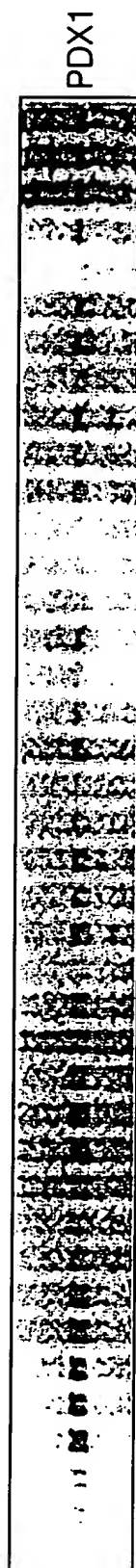


Fig. 6D



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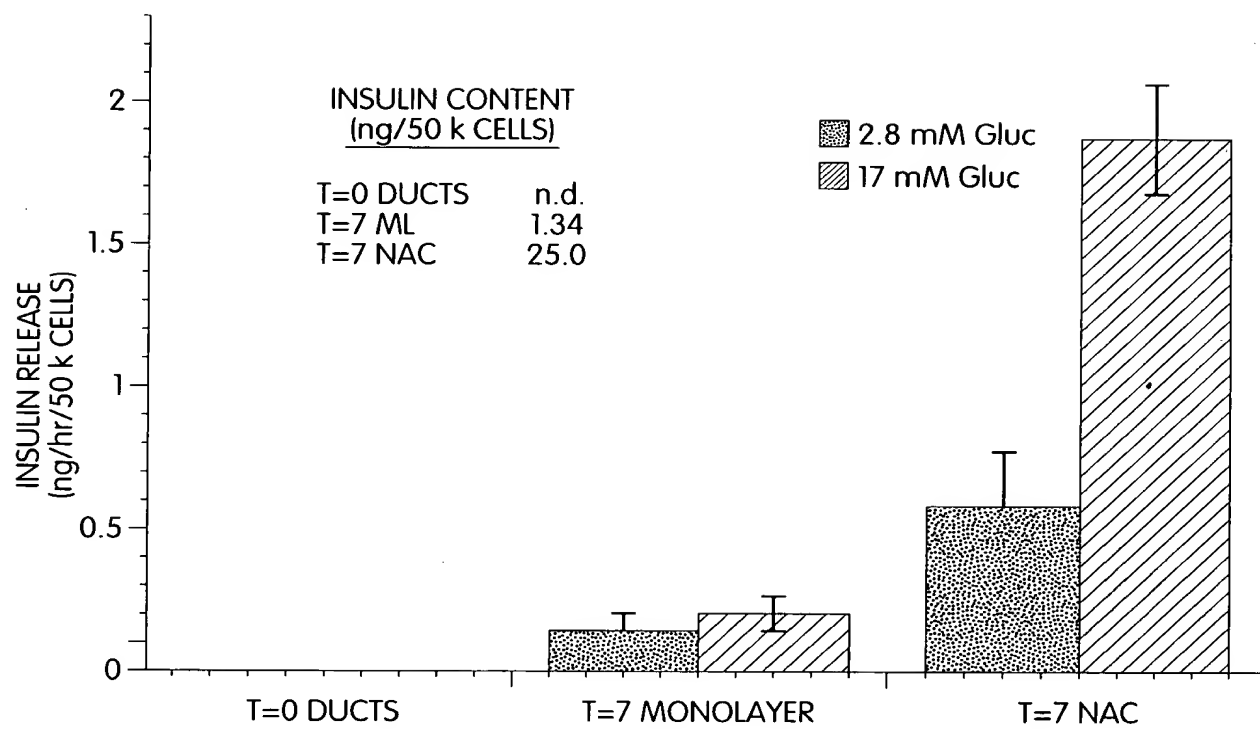


Fig. 7



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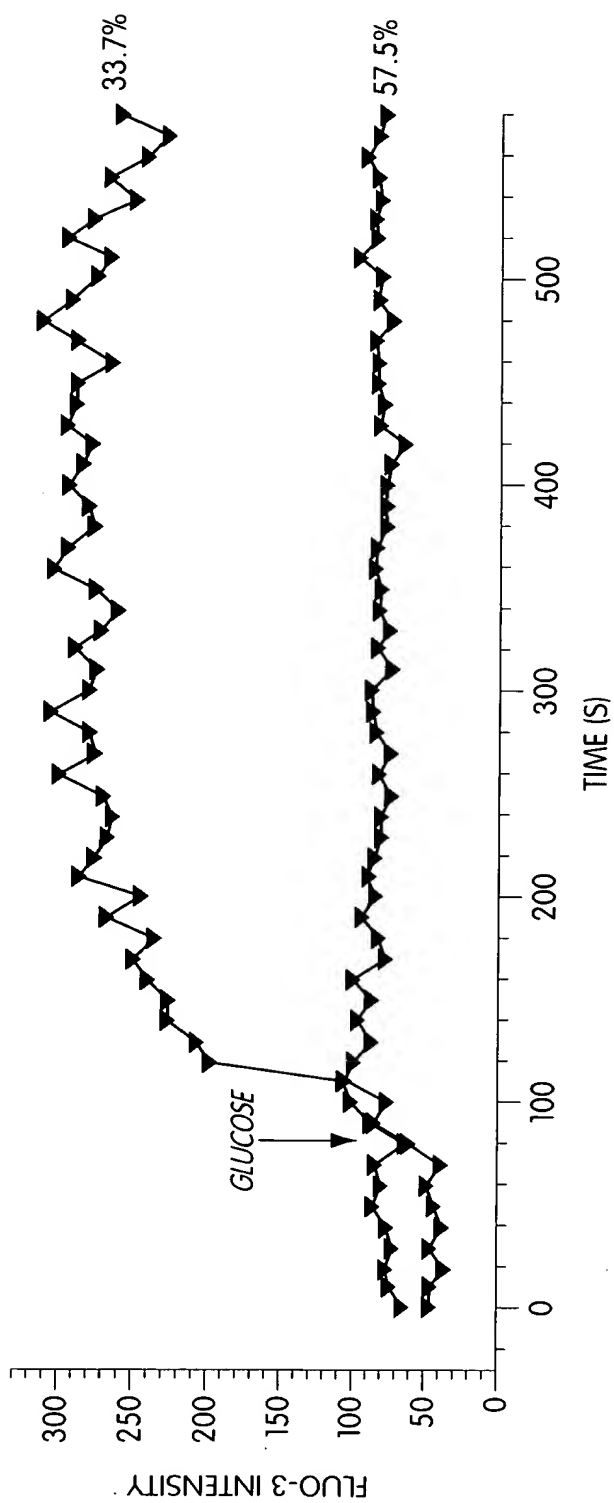


Fig. 8A



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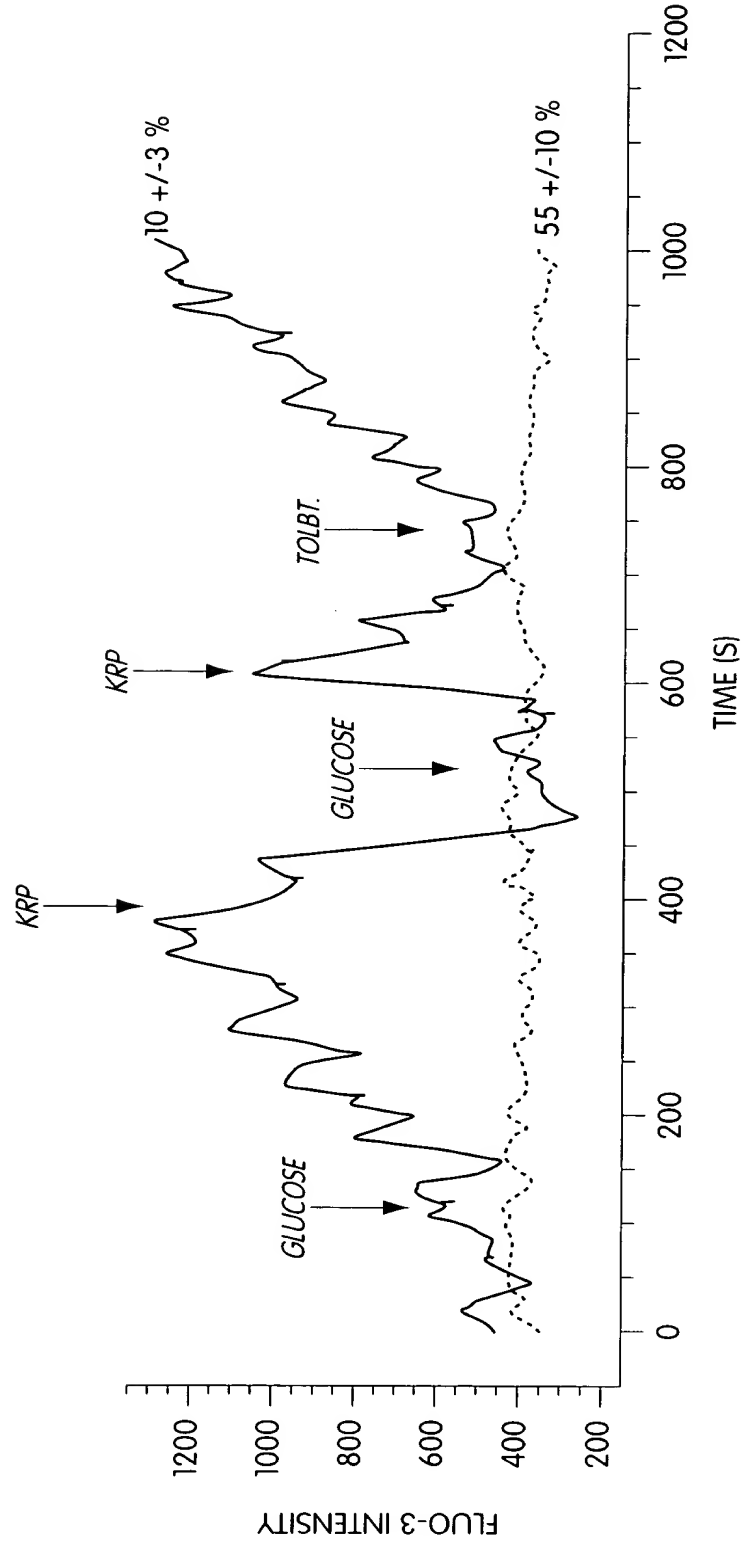


Fig. 8B



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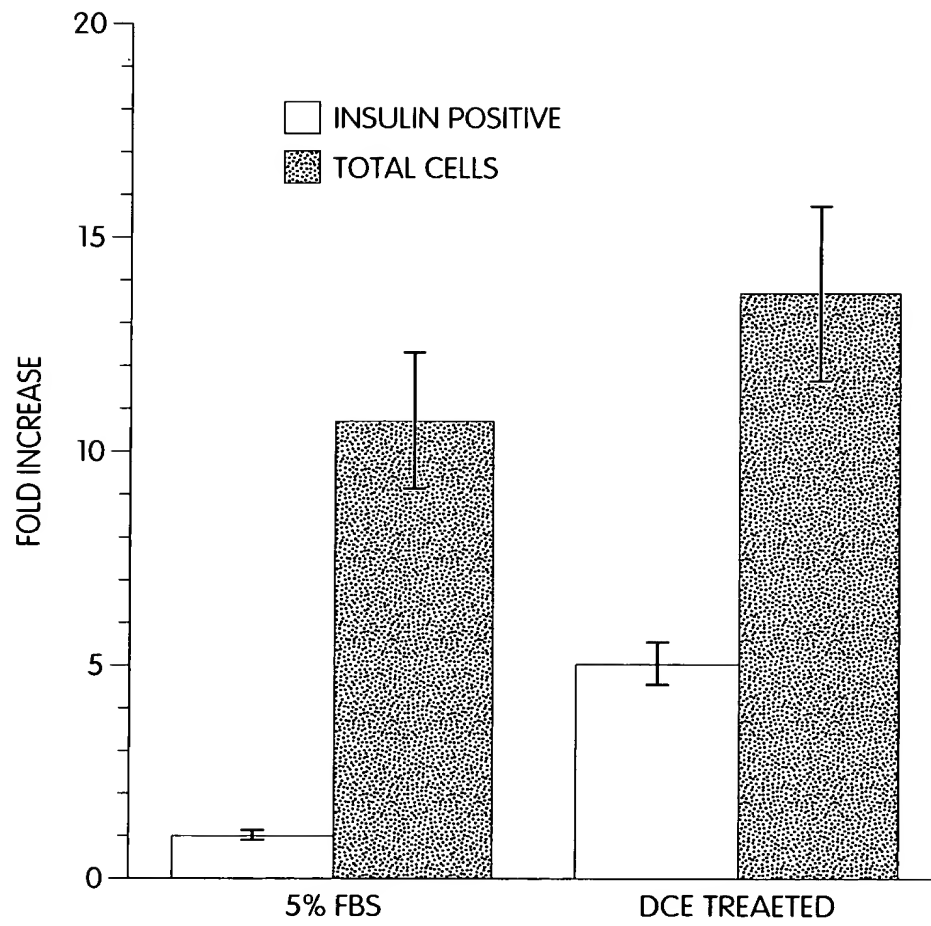


Fig. 9



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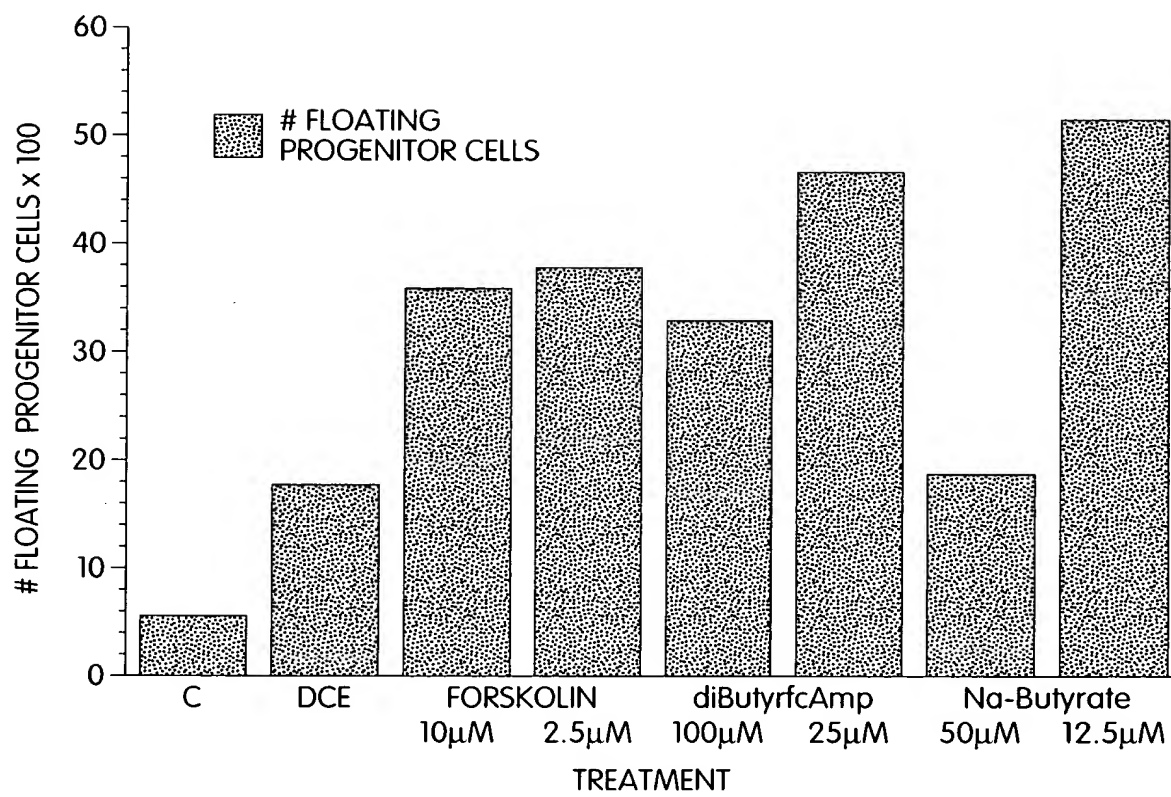


Fig. 10



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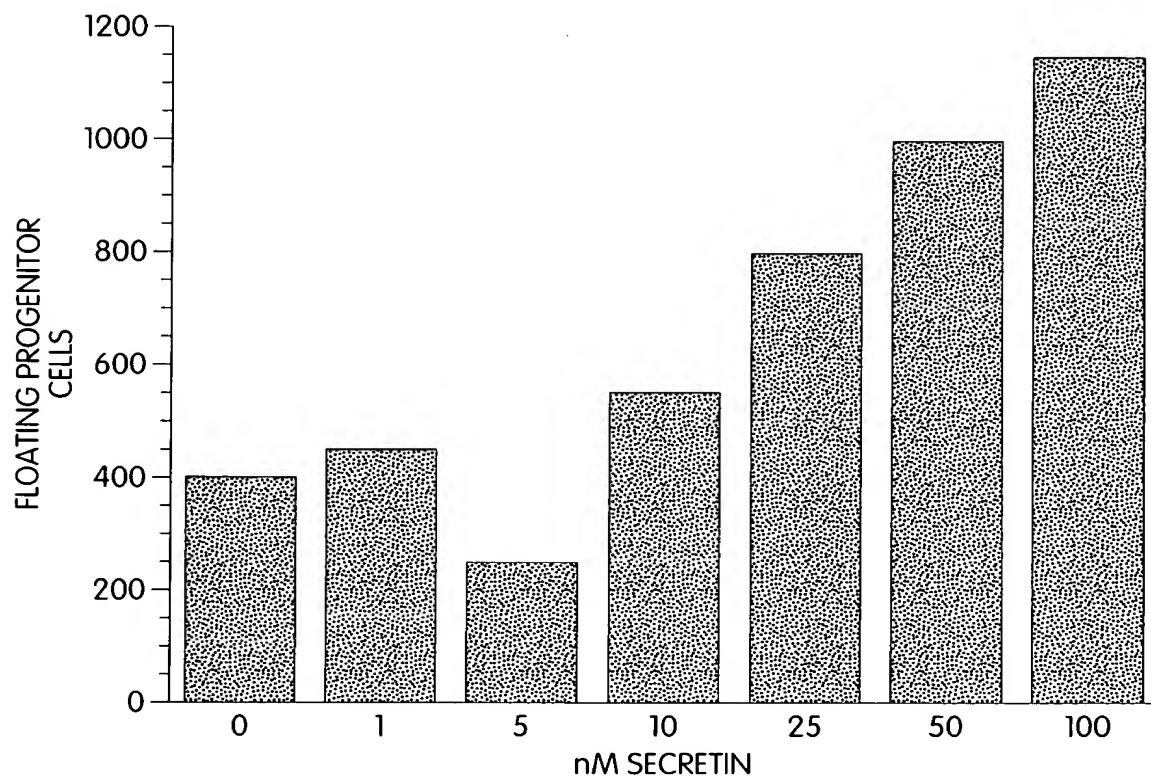


Fig. 11





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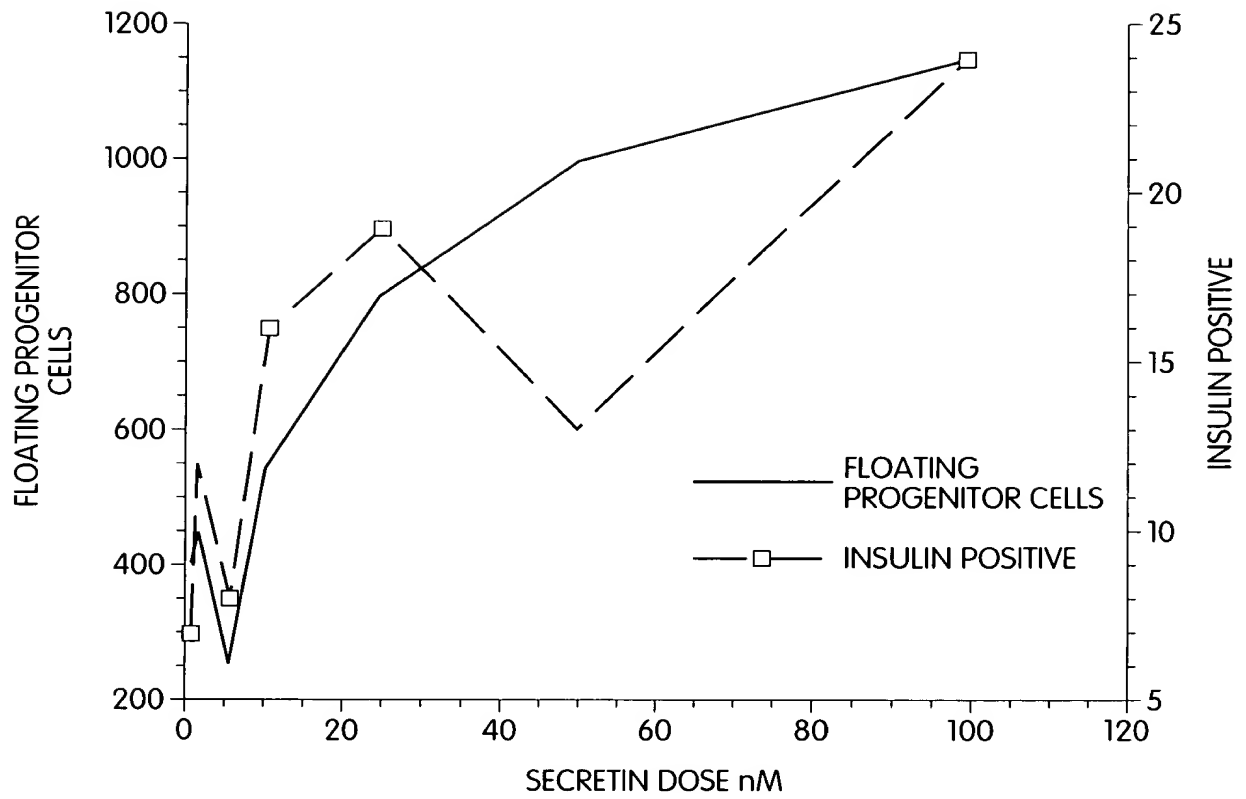


Fig. 12



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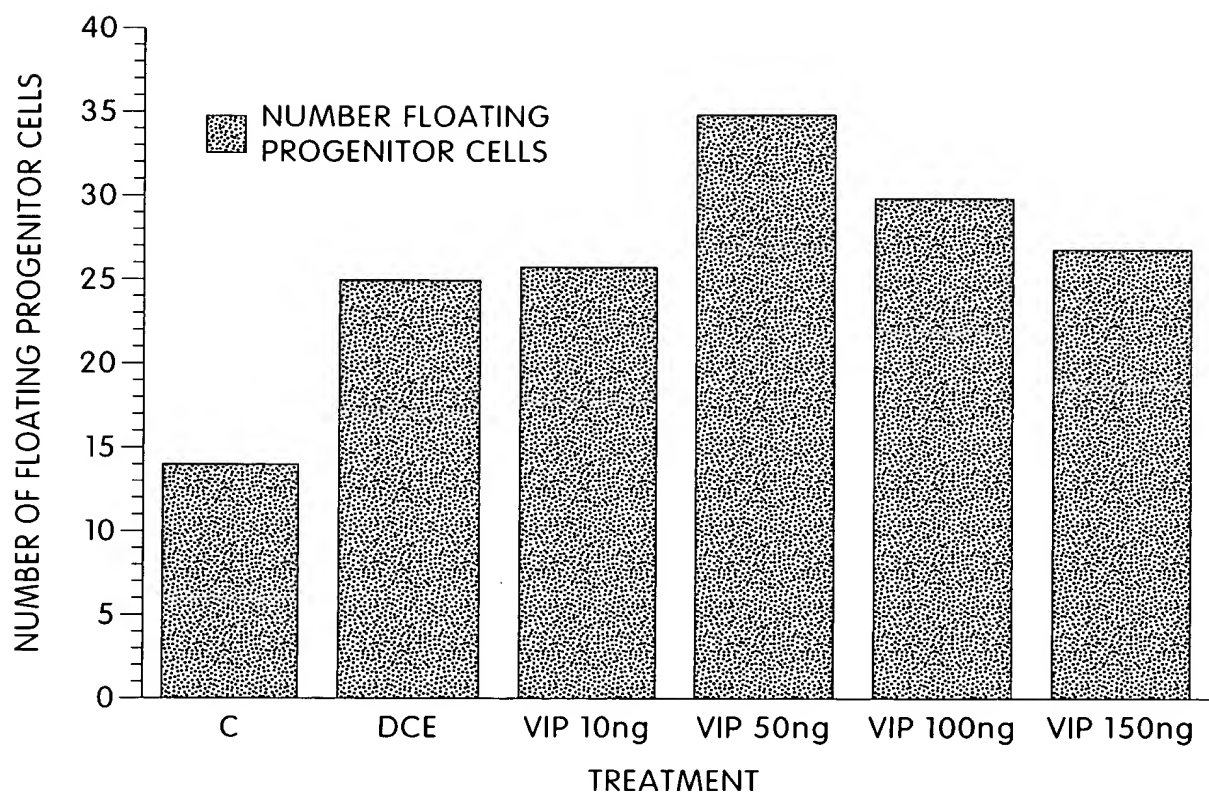


Fig. 13



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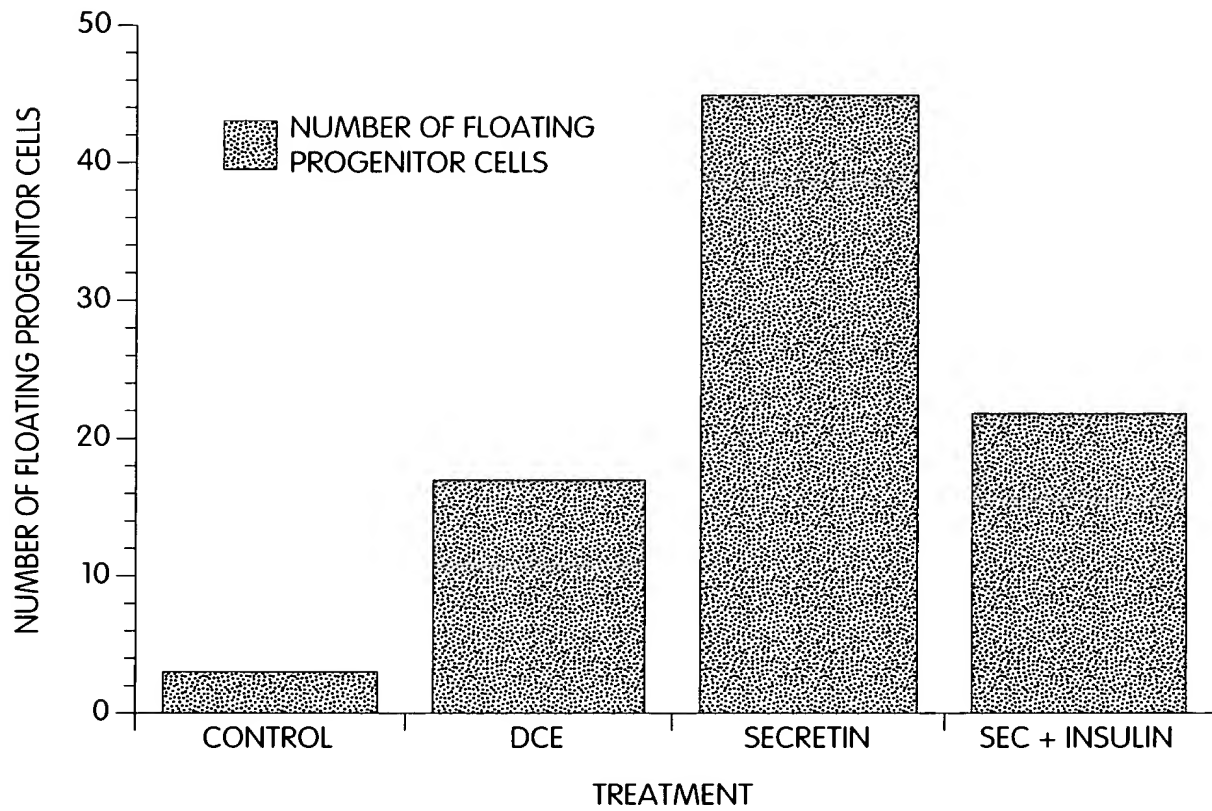


Fig. 14

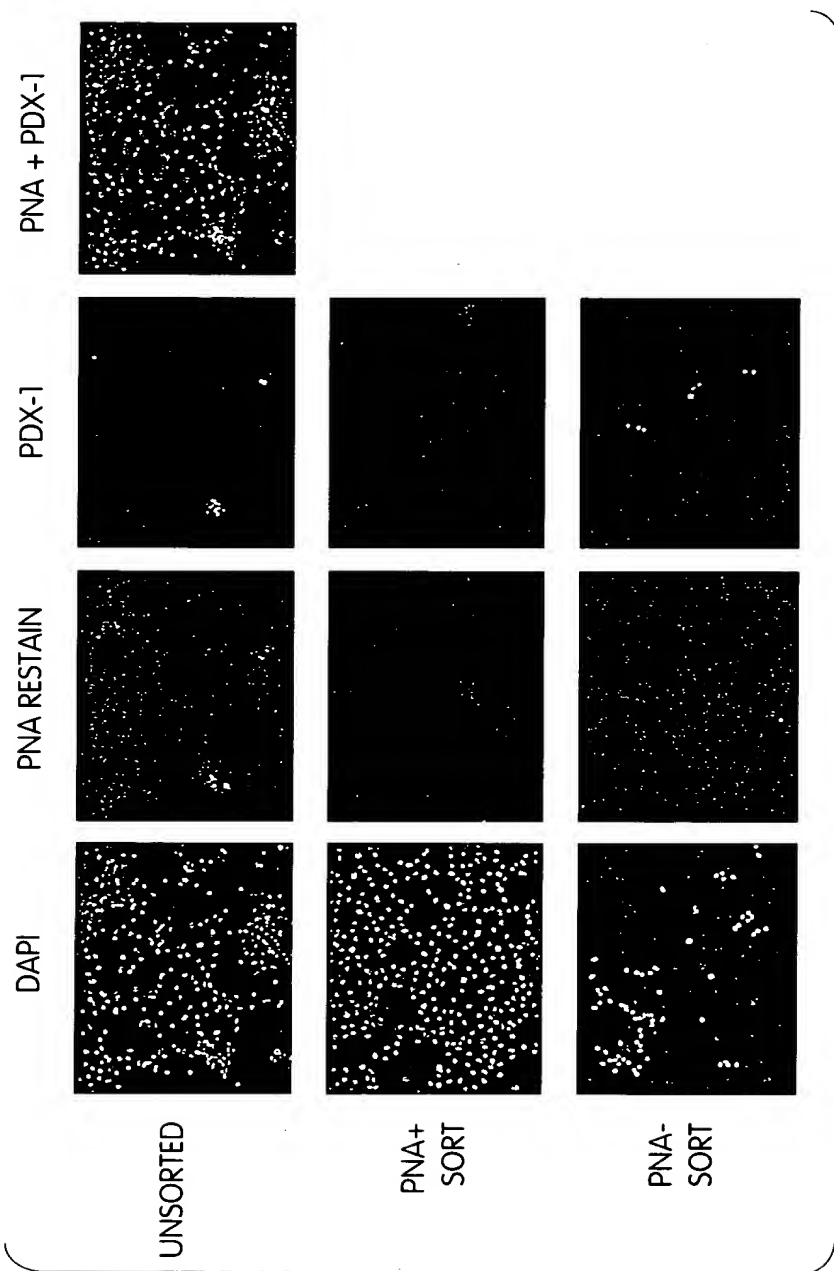


Fig. 15

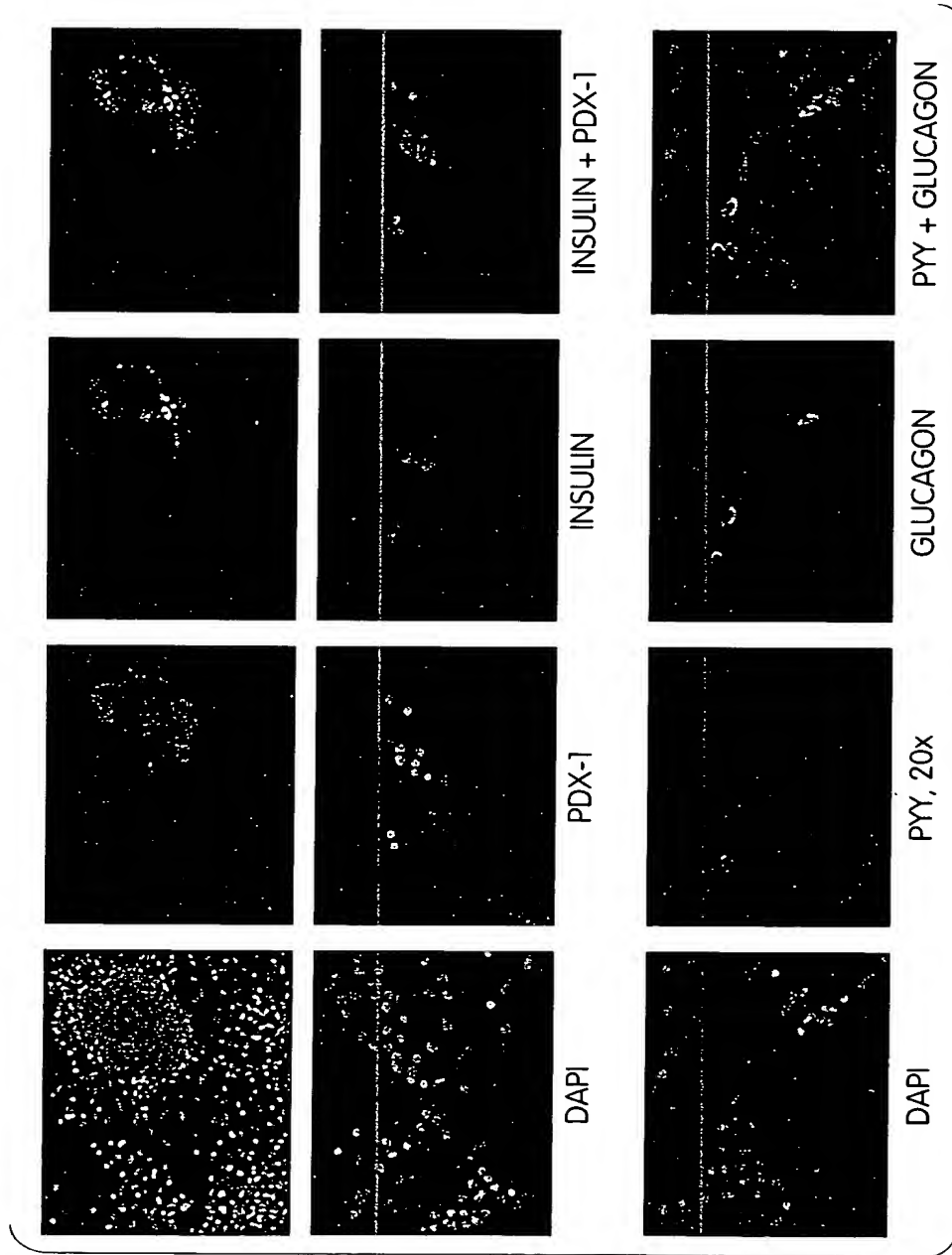


Fig. 16

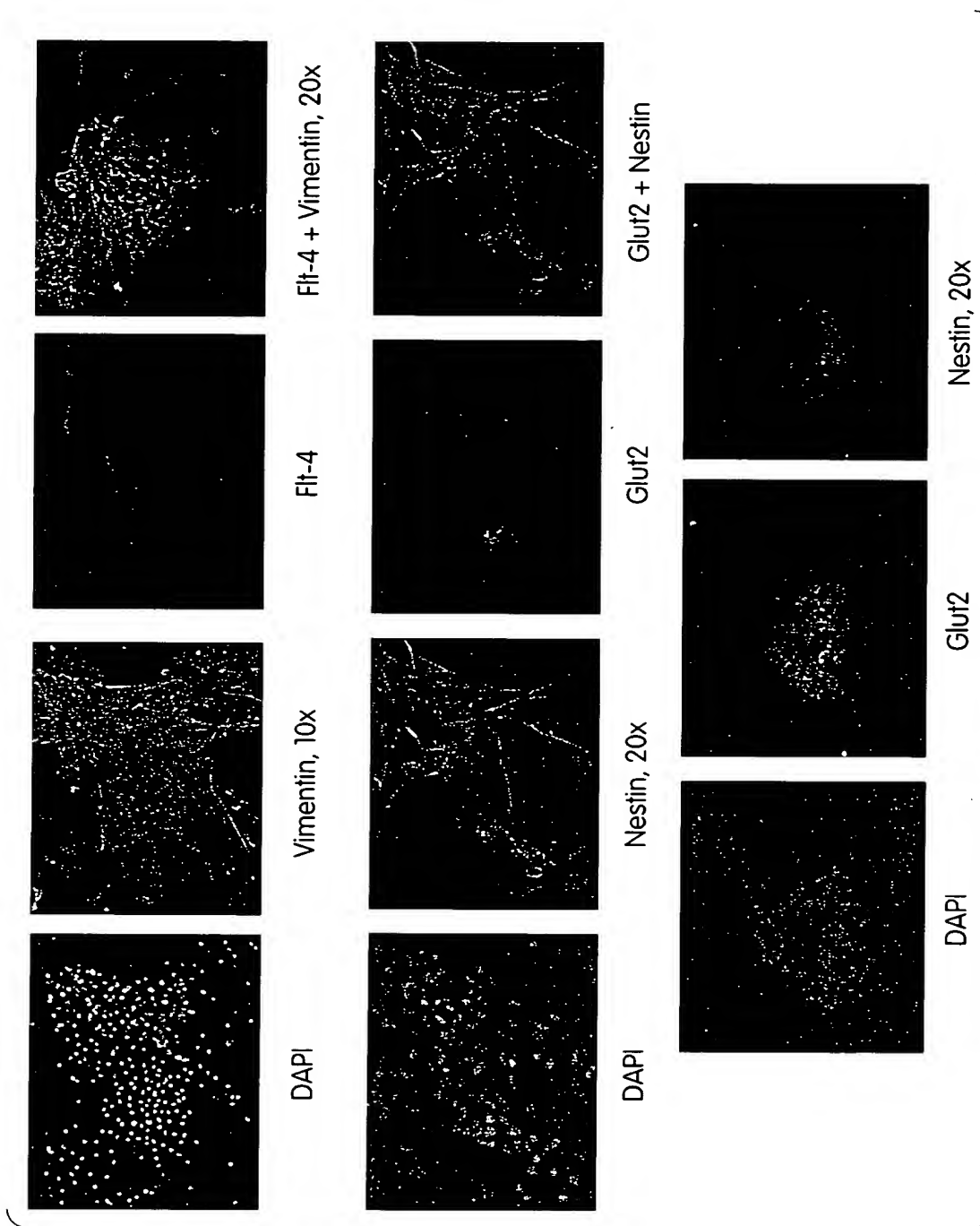


Fig. 17



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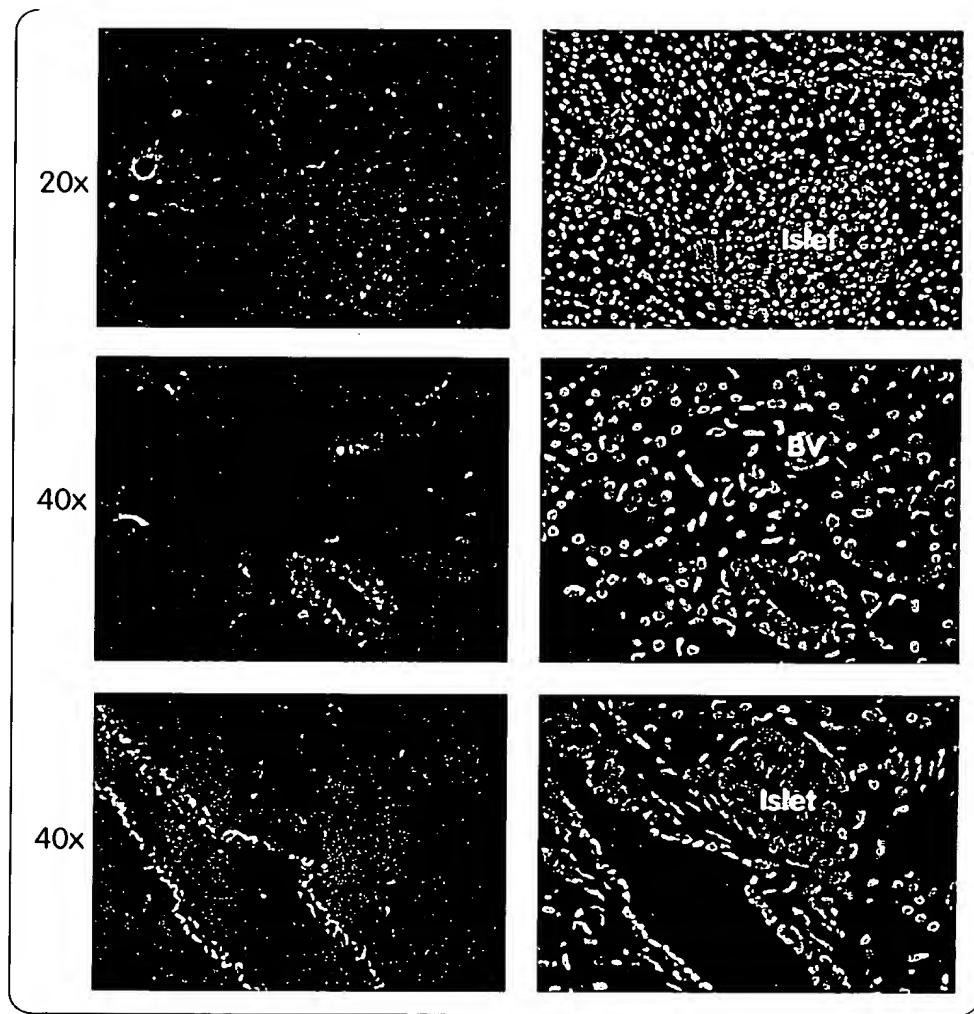
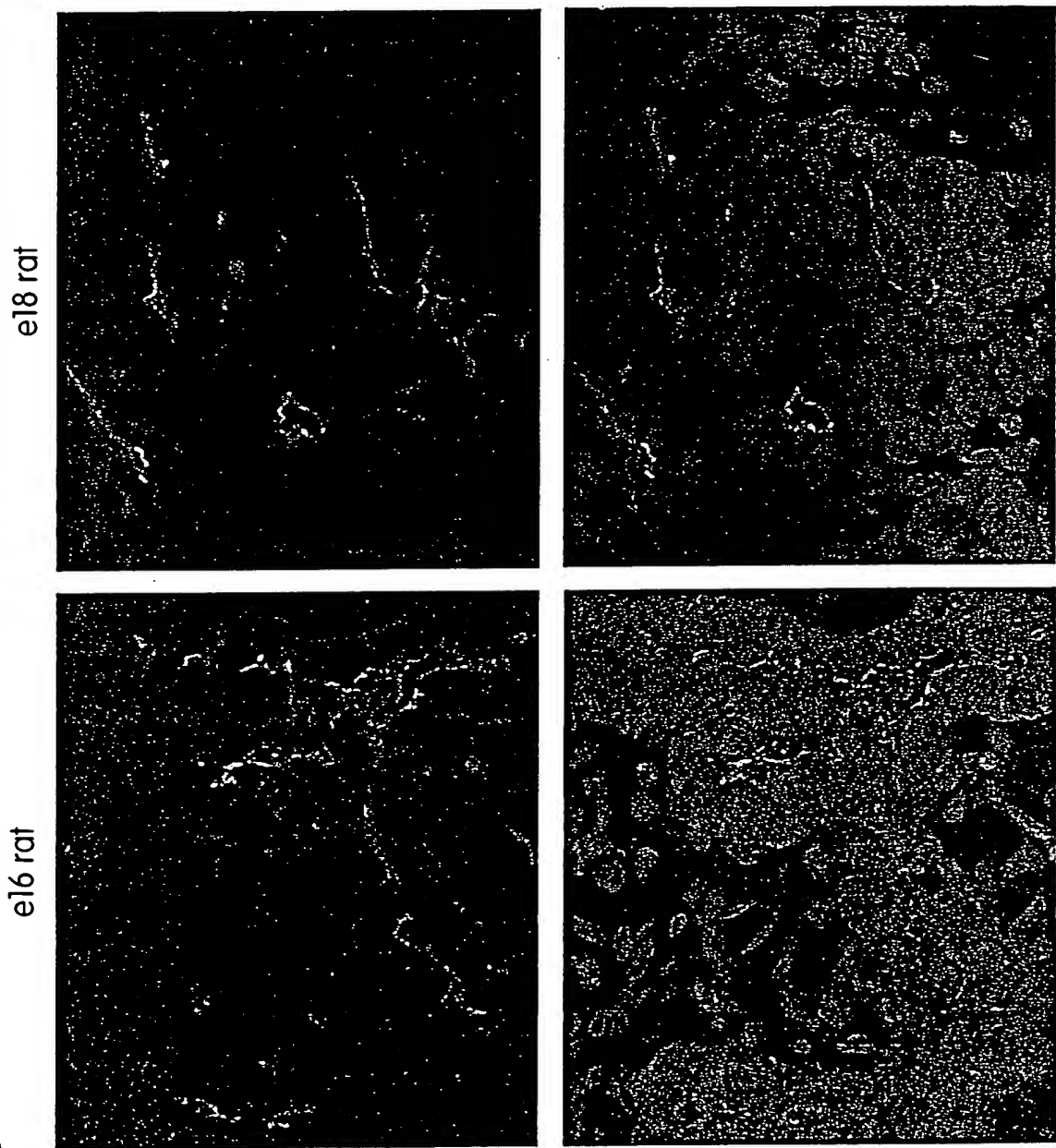


Fig. 18





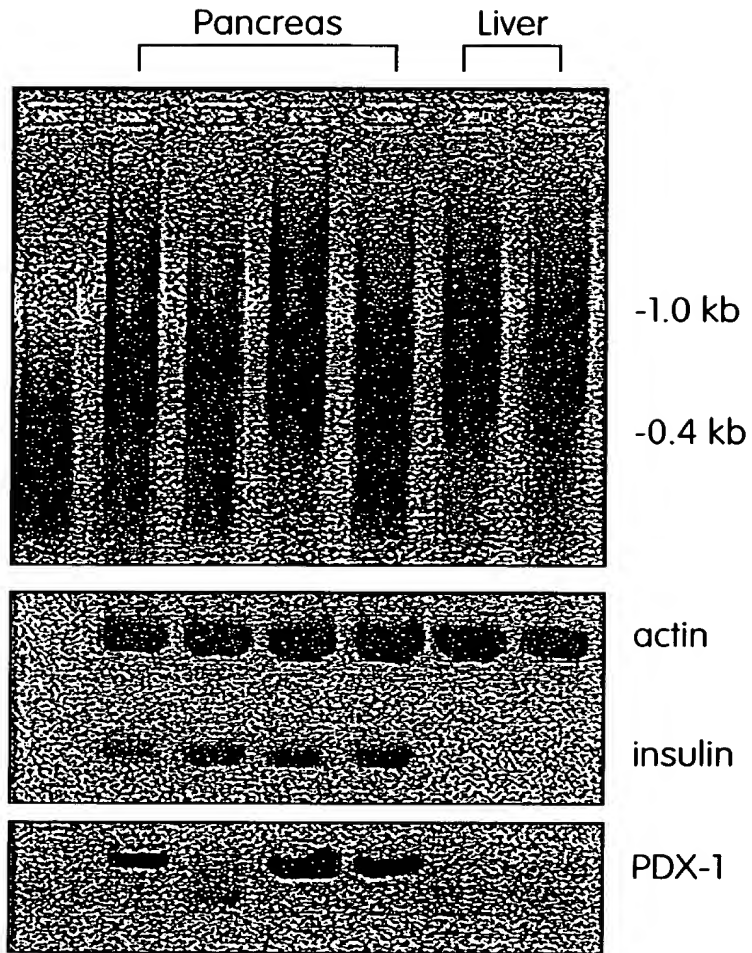


Fig. 20



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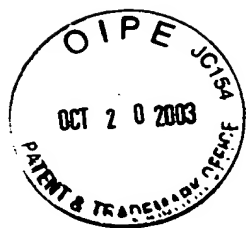
	E13			E14			E15			E16		
	#6	#7	#11	#4	#8	#14	#7	#8	#14	#23	#24	#30
INSULIN	-	-	+	+	+	-	+	+	-	+	+	-
PDX-1	+	+	-	+	-	-	+	-	-	-	-	-
GLUCAGON	±	±	+	+	±	-	-	-	-	-	-	-
AMYLASE	+	±	±	+	+	±	+	+	+	±	+	+
ACTIN	+	+	+	+	+	+	+	+	+	+	+	+
CYCLOPHILIN	+	+	+	+	+	+	+	+	+	+	+	-

Fig. 21

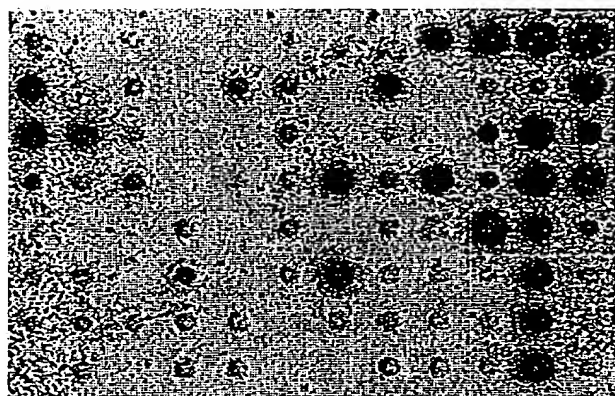


	1	2	3	4	5	6	7	8	9	10	11	12
A	actin	HexoK	PYY	TyrH	SHH	Wnt3	delta	IGF1	TNFR2	PICK1	amphy2	Rho-GDI
B	G3PDH	SubPR	NPY	Rab3A	Patch-1	Wnt5	Jagged	PKA	Pw1	PCTA-RE1	OSF-1	Sez-12
C	G6PDH	insulin	NPYR	activin	SMO	frizzled	DLK	Isl-1	HNF1 $\alpha$	Gli	GP106	SelenoP
D	RPs6	glucagon	Secretin	follicstatin	TGF $\beta$ 1	sFRP-1	notch-1	beta2	DCoH	P48	HCNGP	Surf-1
E	Glut4	SomS	nestin	activinR	TGF $\beta$ 2	EGF	notch-2	PDX1	HNF3 $\beta$	ID-1	clusterin	VASP
F	albumin	PP	Chromo graninA	BMB4	TGF $\beta$ RI	EGFR	FGF6	Pax4	HNF4 $\alpha$	IDR	Cab45b	UK-2
G	amylase	IAPP	GLP-IR	BMB4R	PTHrP	SCF	FGF9	Pax6	Nkx2.2	MITF	HBP	UK-4
H	CarbP	Glut2	CK19	BMB6	PTHR	c-Kit	FGFR1	COUP-TFII	Nkx6.1	SUG1	RP2	UK-6

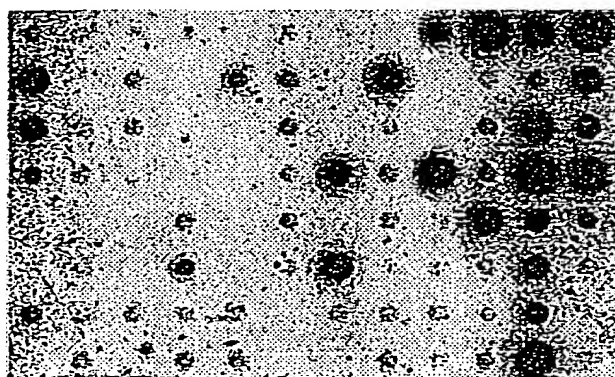
Fig. 22



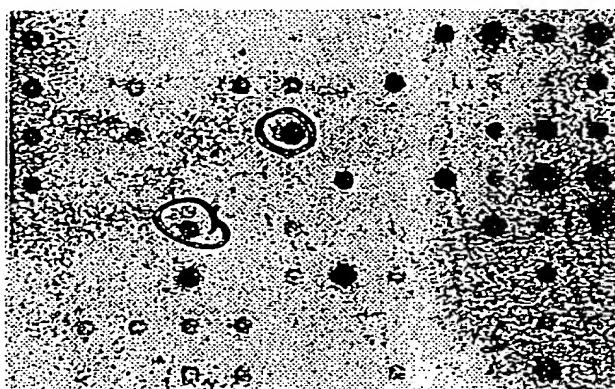
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islet



E15 ins+/PDX+



heart

Fig. 23



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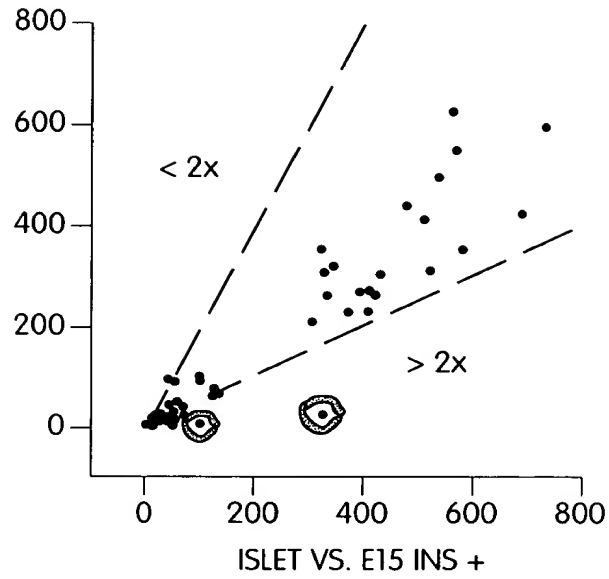


Fig. 24A

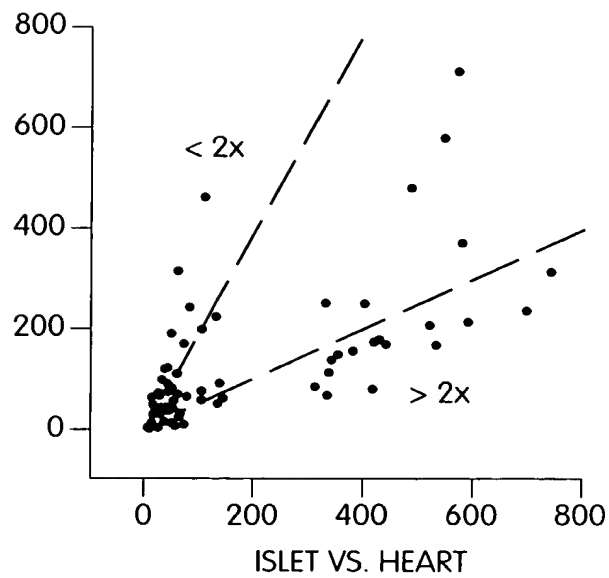


Fig. 24B



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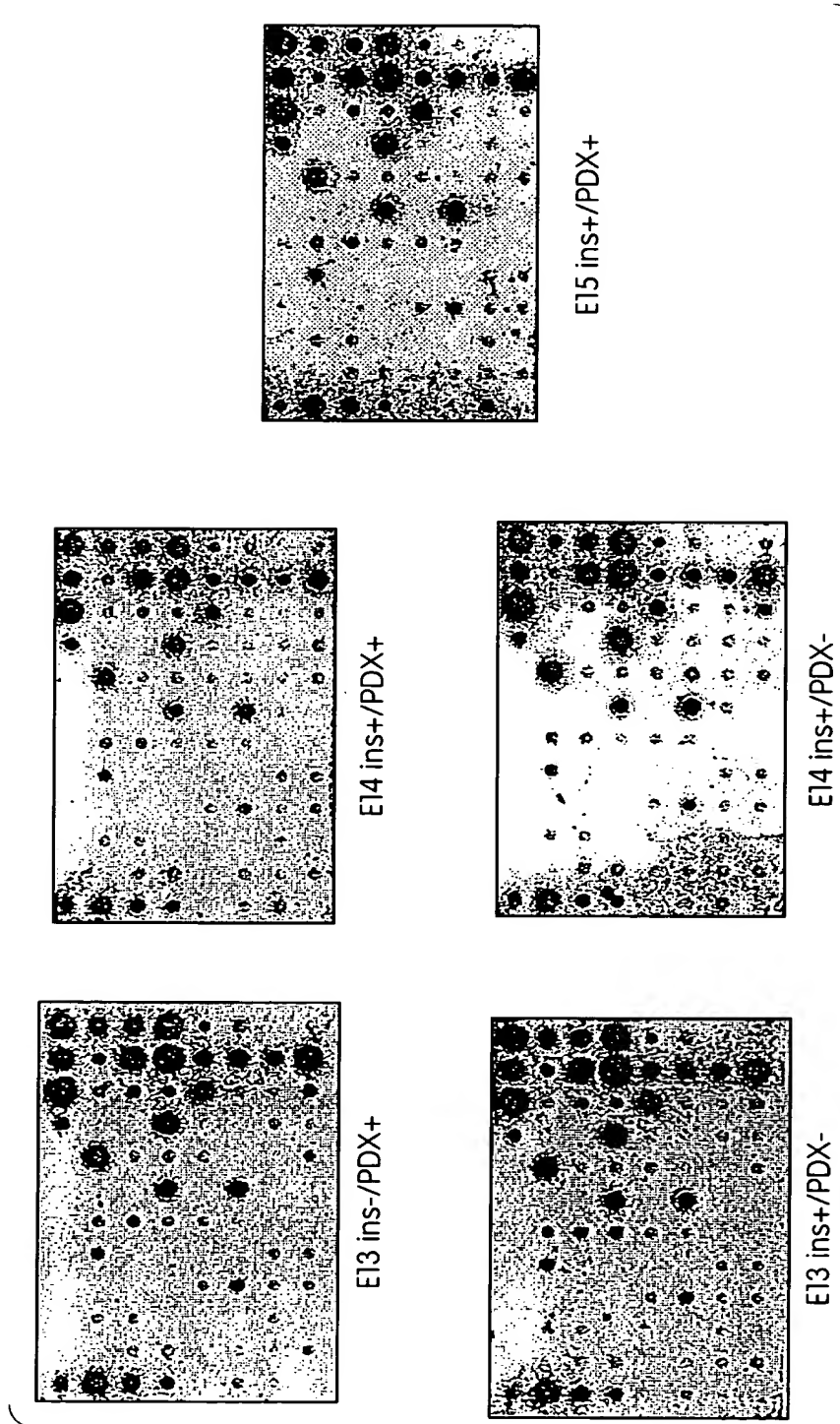


Fig. 25



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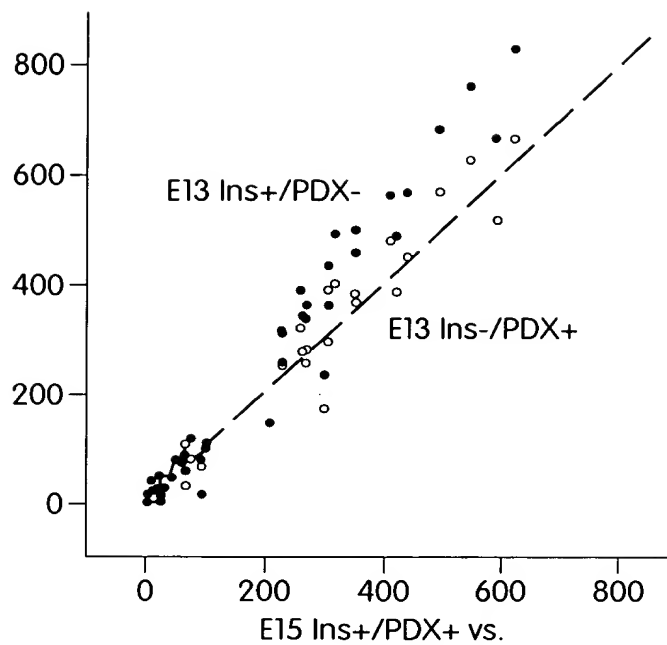


Fig. 26A

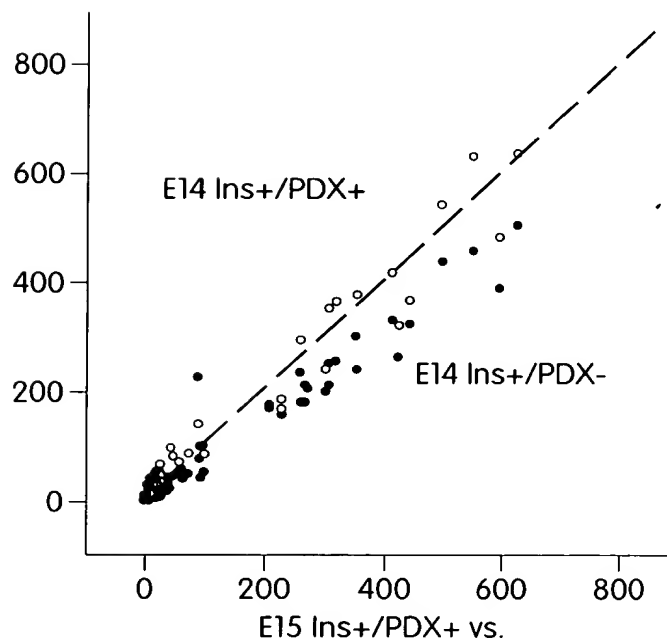


Fig. 26B

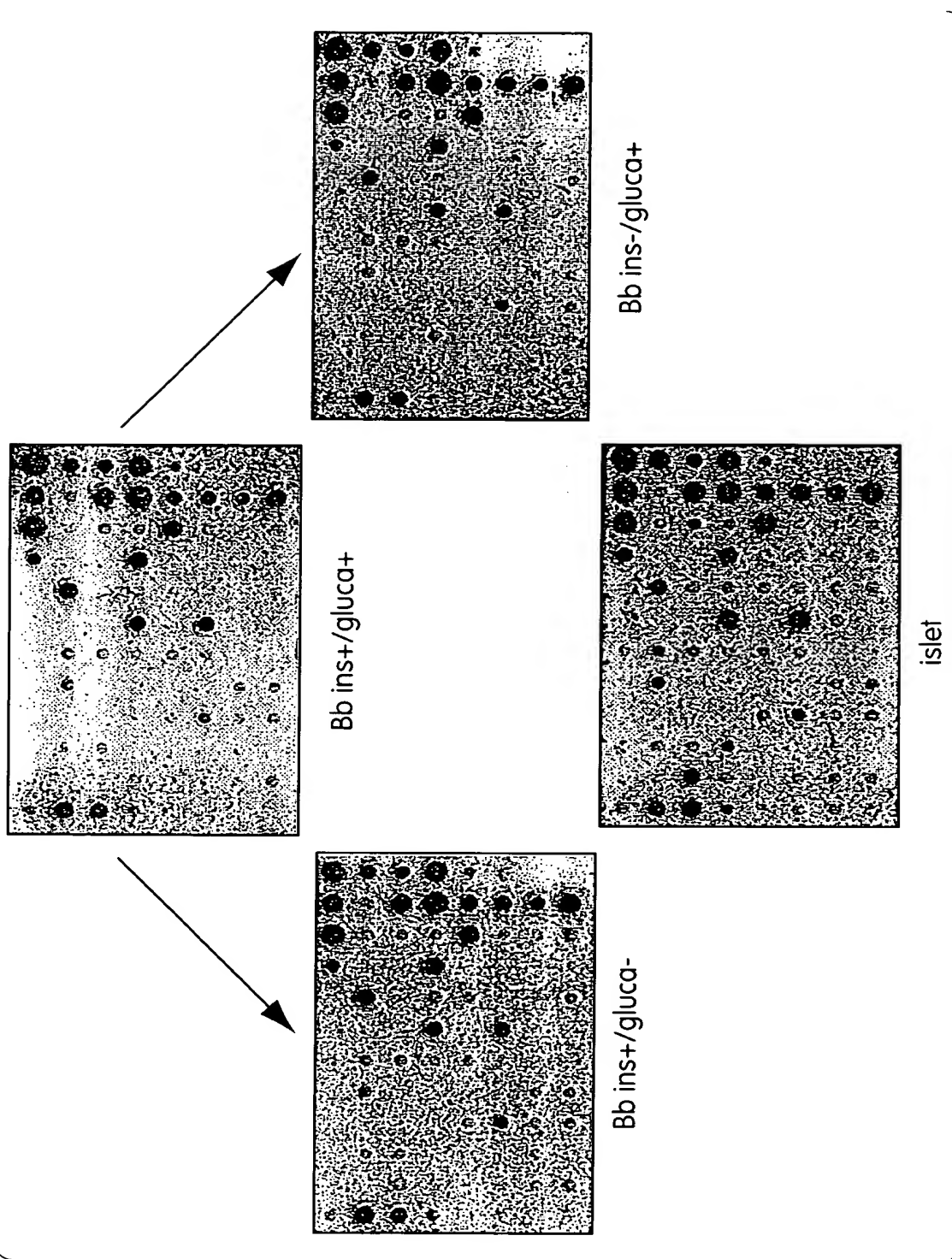


Fig. 27





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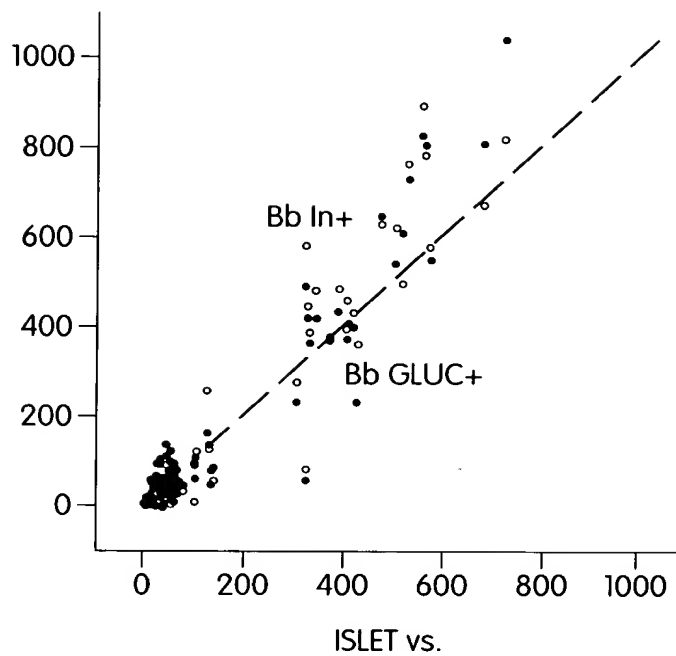


Fig. 28A

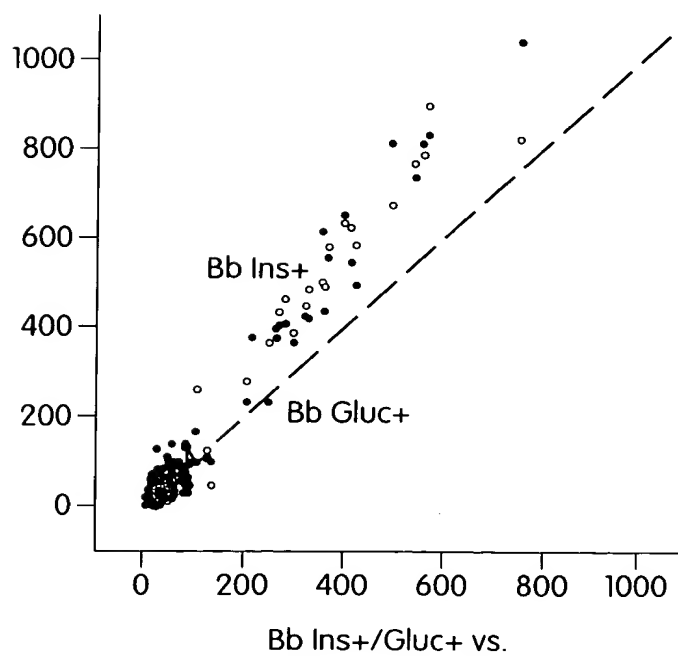


Fig. 28B



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<u>GENE NAME</u>	<u>ISLET/E15 Ins+</u>	<u>ISLET/Bb Ins+</u>
Secretin	16	8
insulin	13	4
glucagon	3	2
IGF1	6	6
nestin	5	3
Rab3A	5	2
Glut2	2	1.3
ChromograninA	4	3
PDX1	3	2
Isl-1	2	2
EGF	4	2
NPYR	4	1.3
TGFb1	4	3
TGFbR1	6	2
delta	26	18
DLK	3	4
Wnt3	3	2
Gli	2	2
SMO	4	6
COUP-TFII	0.9	1.1

Fig. 29



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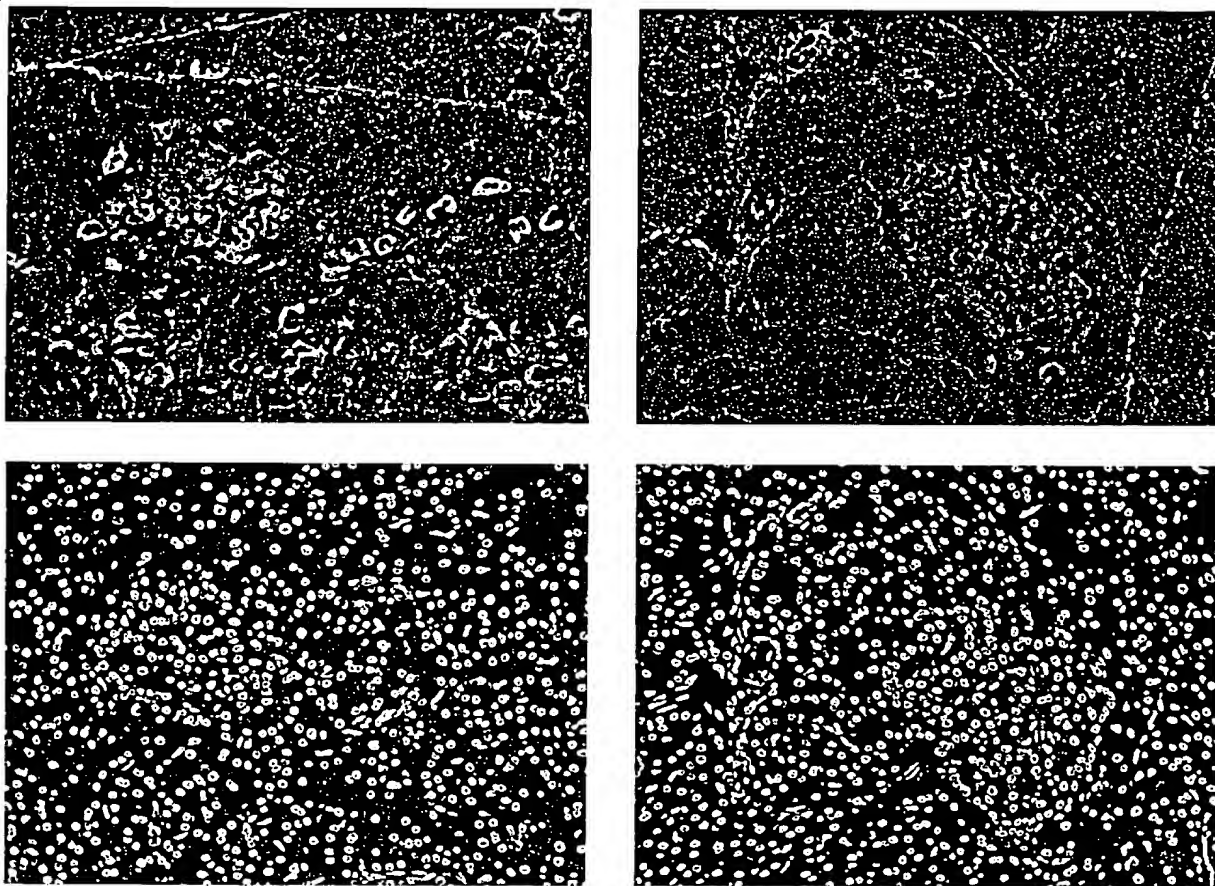


Fig. 30

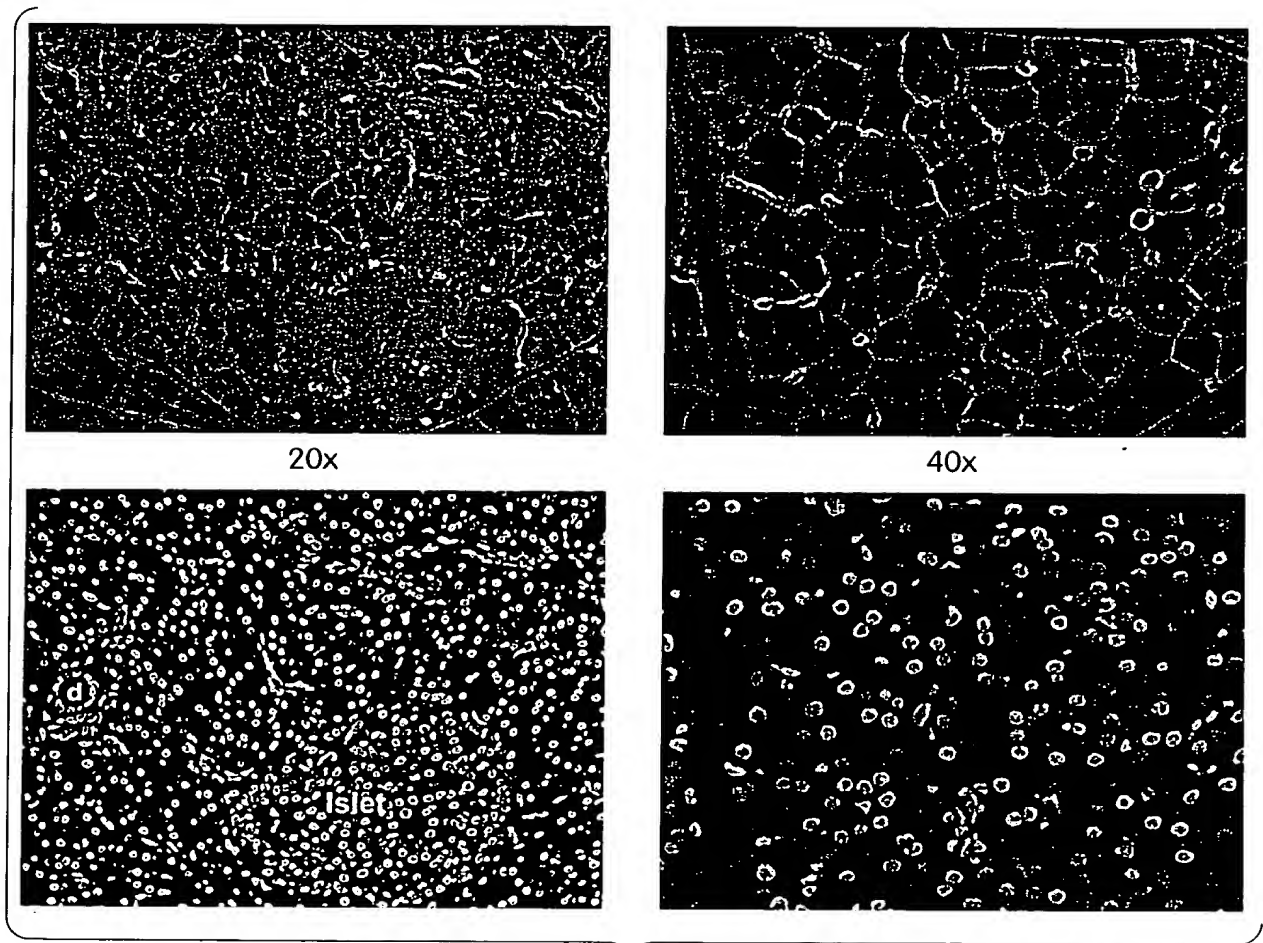
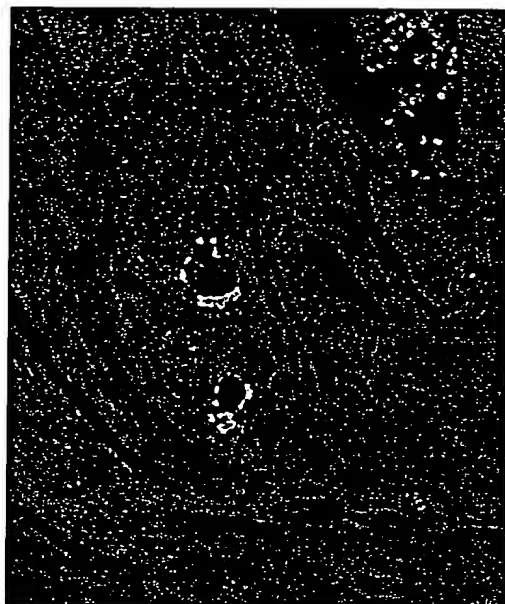


Fig. 31



Subpopulation of Epithelium



Interlobular Duct, 40x



Interlobular Ducts, 20x (Negative)



Positive Epithelial Cells

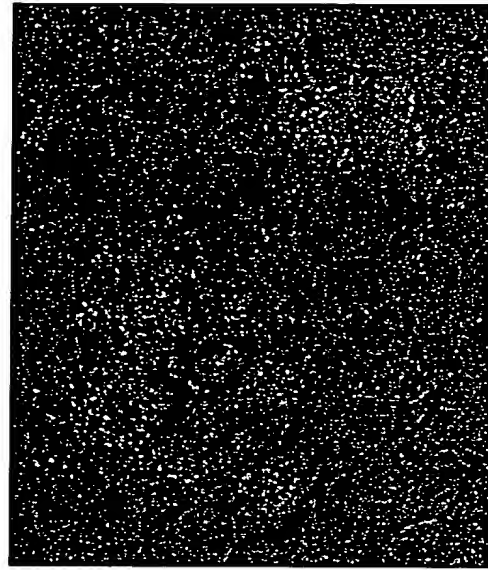
Fig. 32



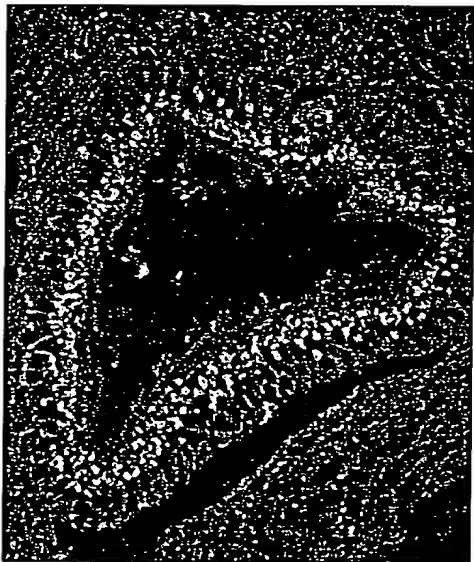
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Interlobular Duct, 20x



Islets, 20x



Interlobular Duct, 40x



DAPI

Fig. 33

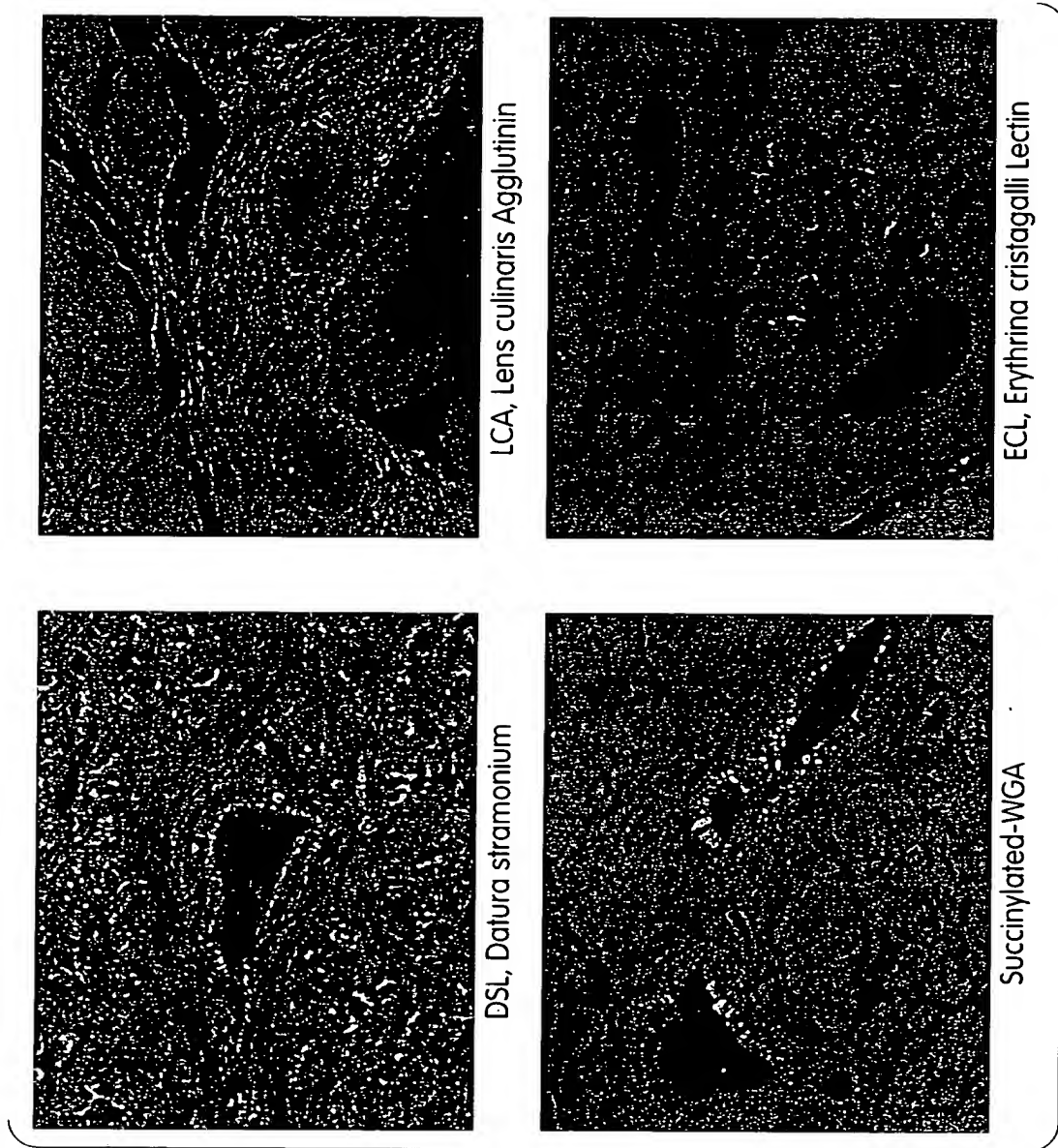
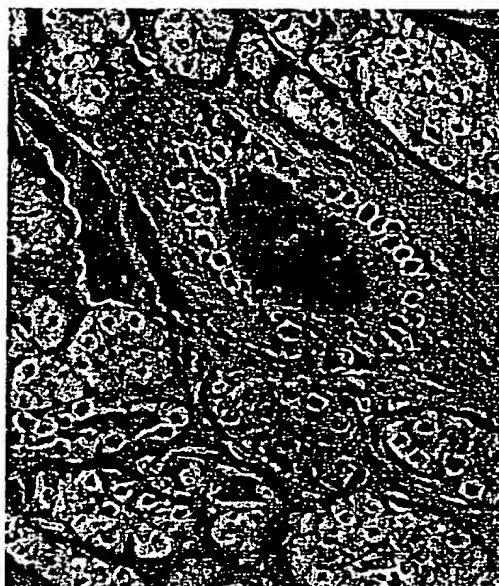


Fig. 34



40x, Interlobular and Intralobular Ducts



20x, Intralobular Ducts

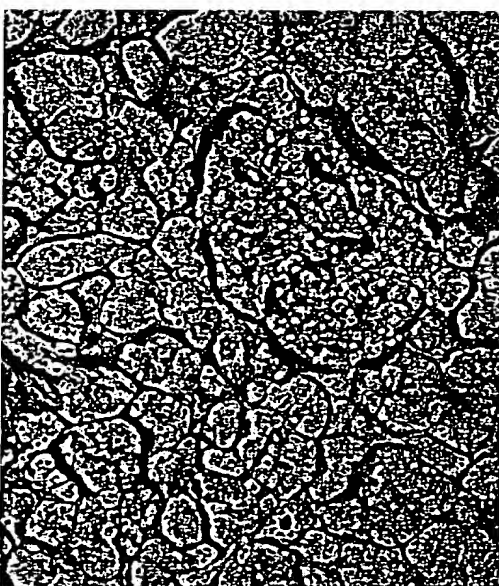
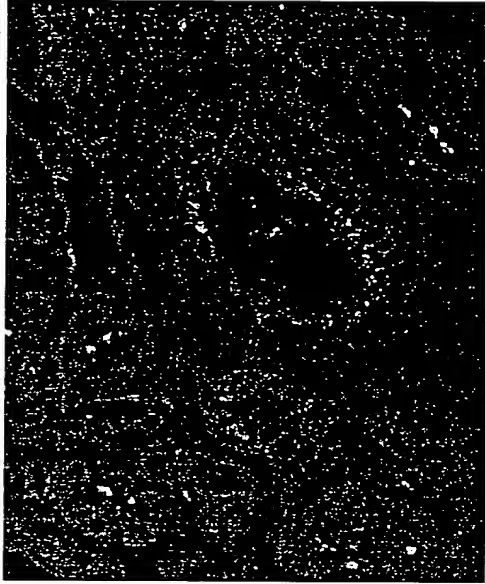
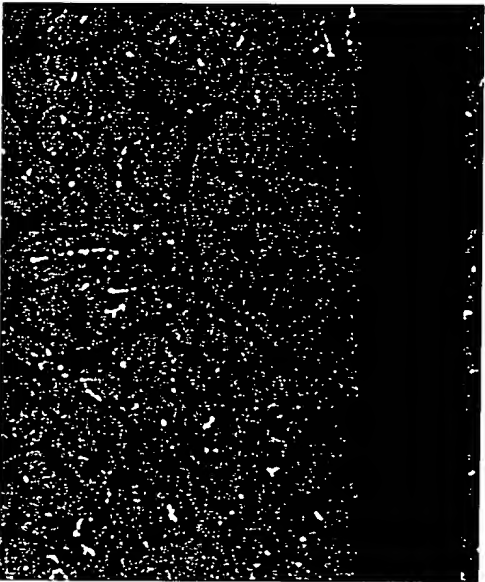


Fig. 35





40x, Interlobular and Intralobular Ducts



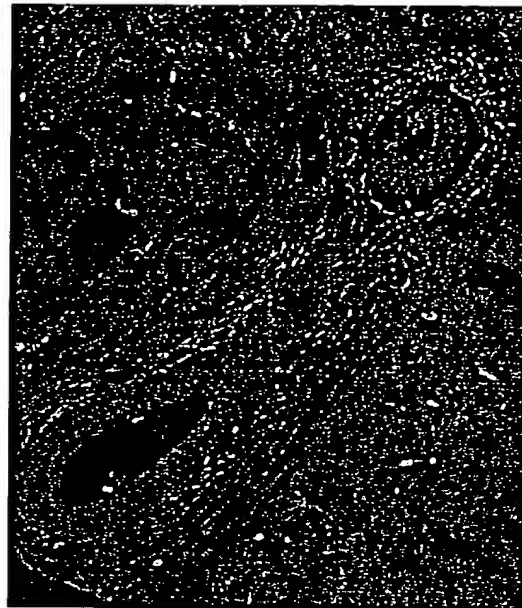
20x, Interlobular Ducts



Fig. 36



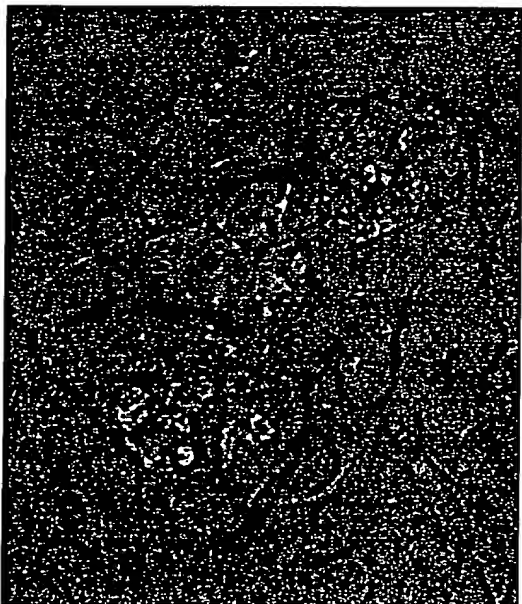
RCA-II, Small Ductules & Mesenchyme



RCA-II, Small Ductules & Mesenchyme

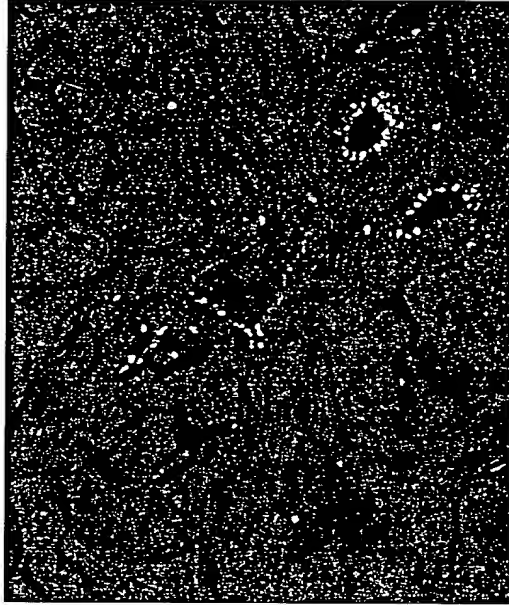


RCA-I, Ducts and Mesenchyme



RCA-II, Islets

Fig. 37



Interlobular Ducts, negative Islet, 20x



Main and Interlobular Ducts, 20x



Duct Epithelium, 20x



Main and Interlobular Ducts, 10x

Fig. 38



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Fig. 39



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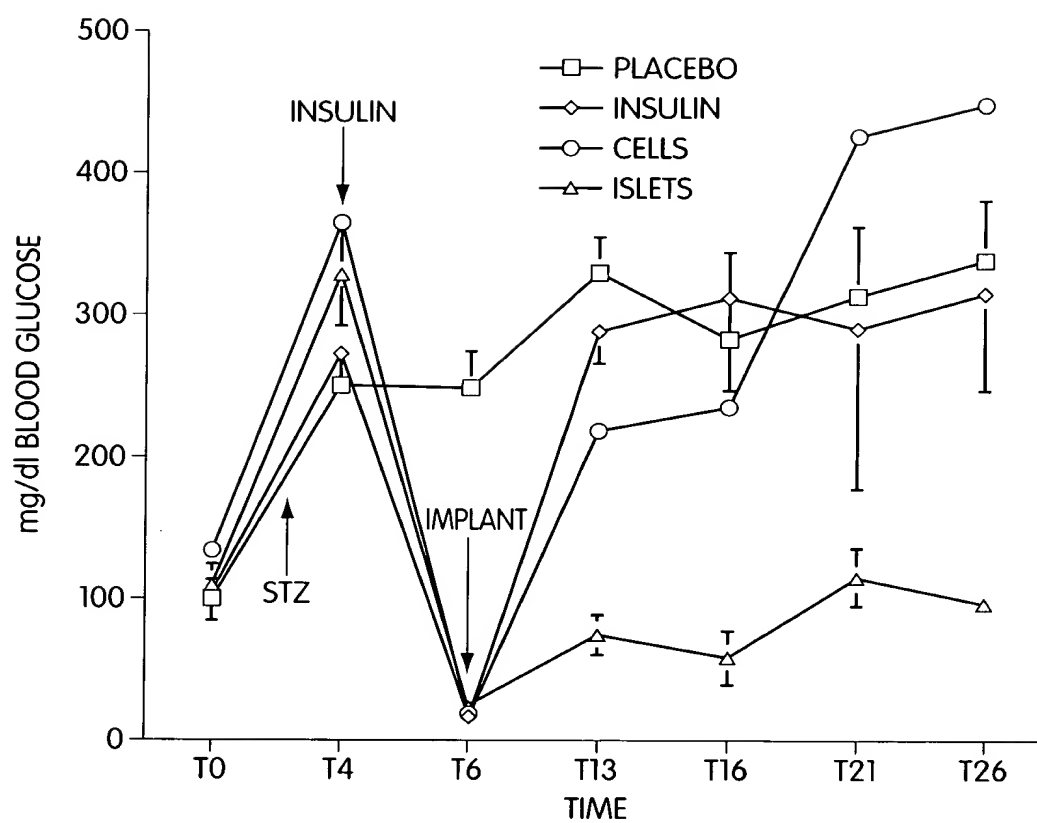


Fig. 40



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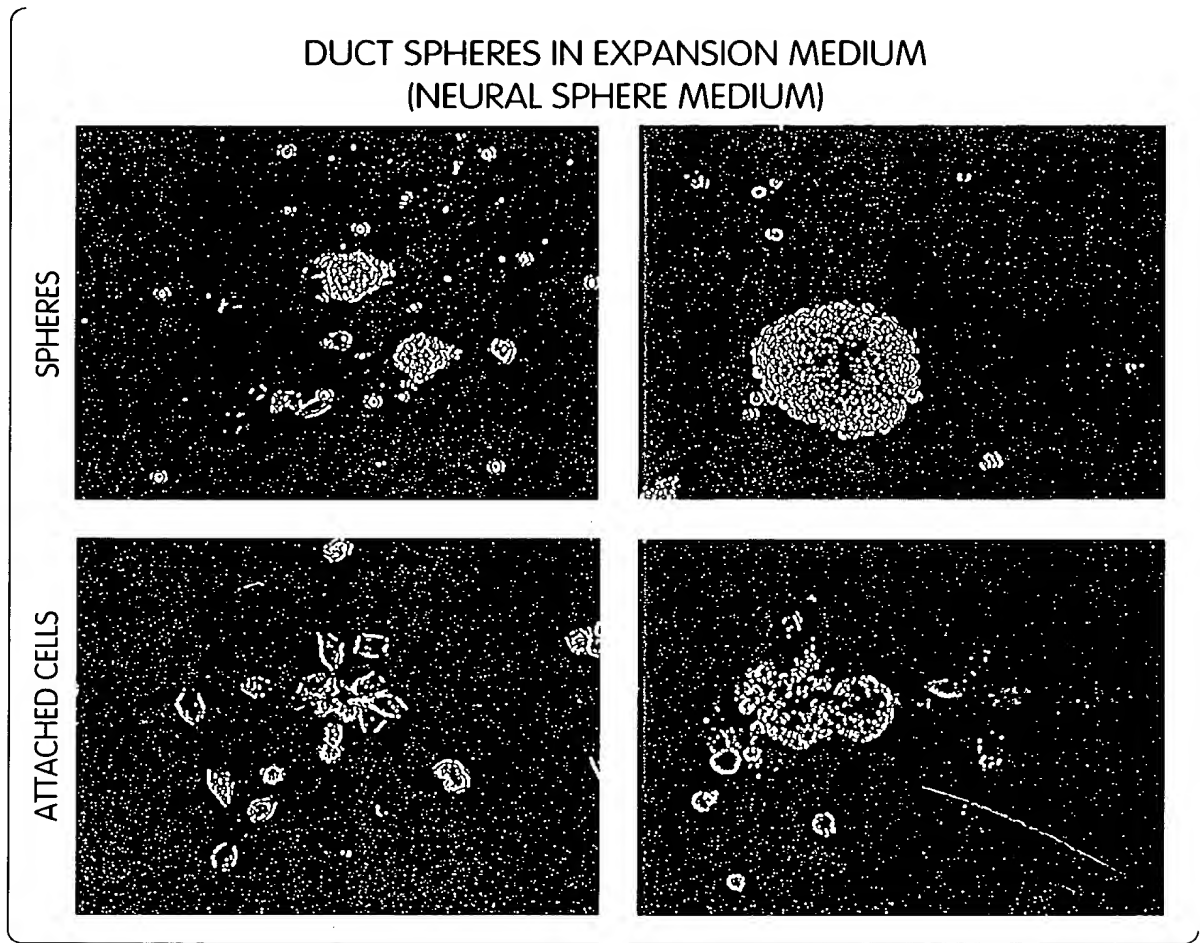
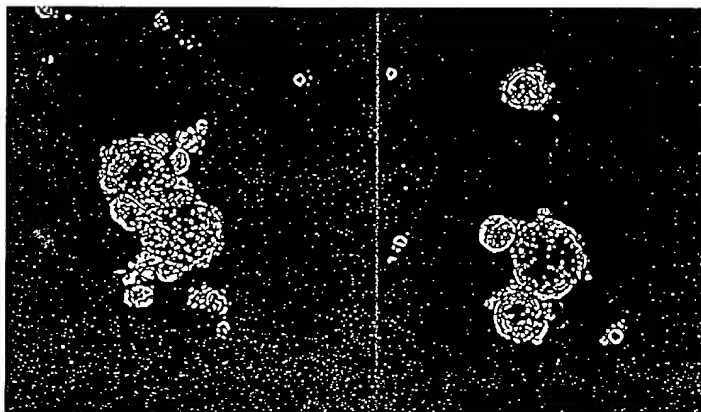


Fig. 41

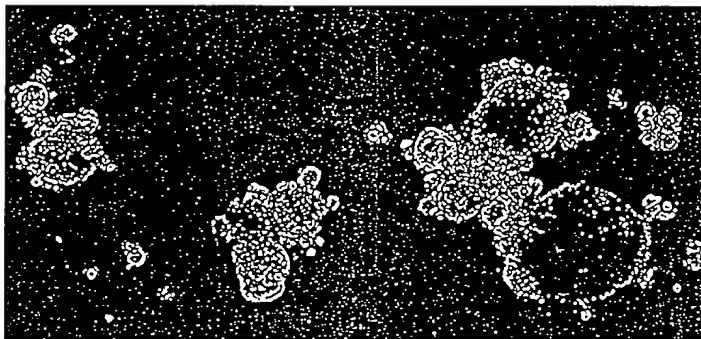
p14 DUCT PREP GROWN IN SPHERE MEDIA  
ON NON-TC SURFACE, p3  
ALL 10x mag.

MEDIA 1  
KO-B  
+15% KO-SR  
+TGF $\alpha$  + HGF  
+ IGF-I&II  
2mM GLUCOSE



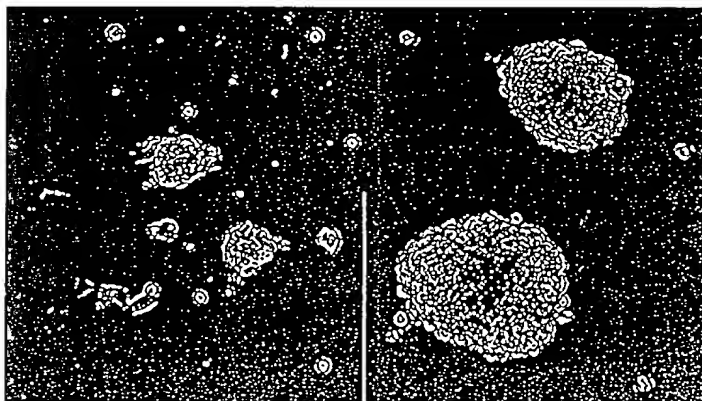
SLOWER GROWTH  
FEWER SPHERES  
HEALTHY

MEDIA 3  
LIVER BASAL  
+15% KO-SR  
+TGF $\alpha$  + HGF  
+ IGF-I&II  
11mM GLUCOSE



VERY FAST GROWTH  
MANY SPHERES  
LESS HEALTHY

NEUROSPHERE  
MEDIUM  
+Ins + EGF  
+bFGF + LIF  
17mM GLUCOSE



VERY HEALTHY  
VERY SLOW GROWTH  
FEW SPHERES

Fig. 42

DUCT SPHERE CELL *IN VITRO* DIFFERENTIATION  
- Glut2 / NESTIN

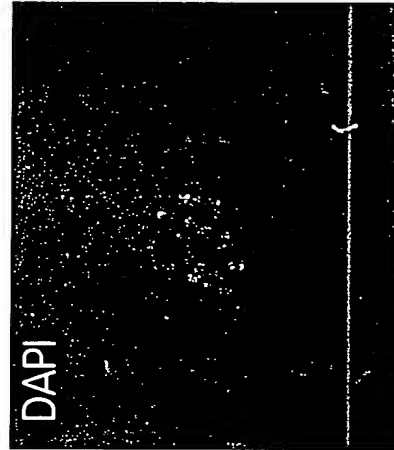
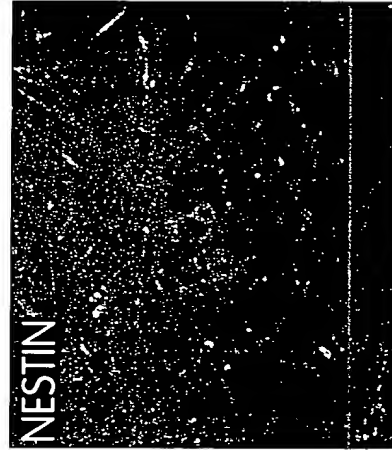
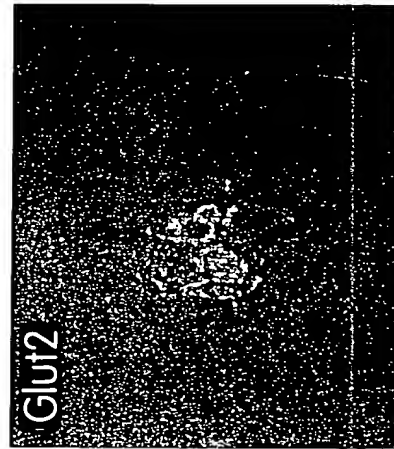
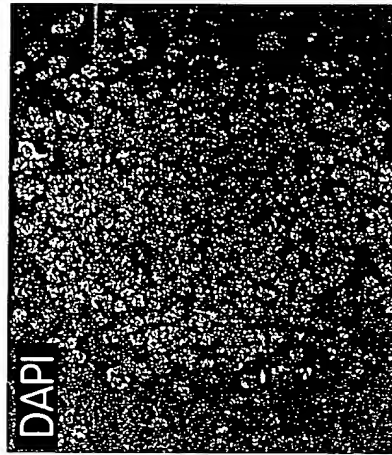
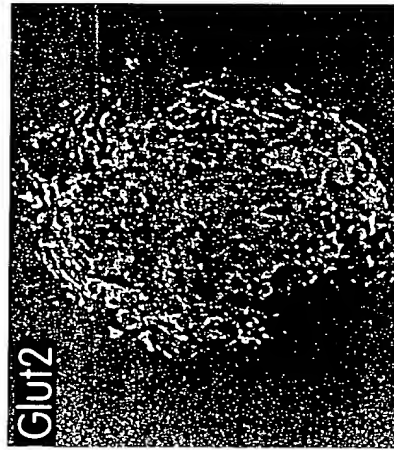
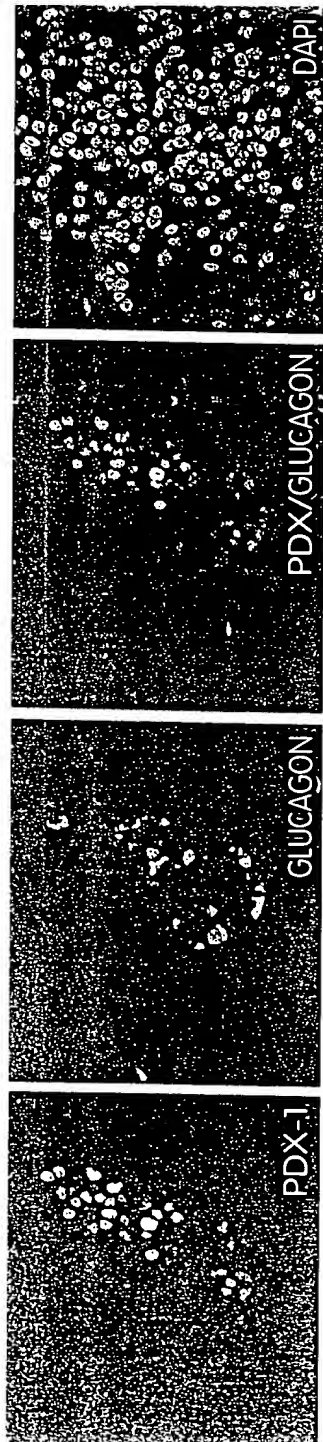


Fig. 43



DUCT SPHERE CELL IN VITRO DIFFERENTIATION  
- PDX / GLUCAGON

SINGLE CLUSTER



TWO CLUSTERS

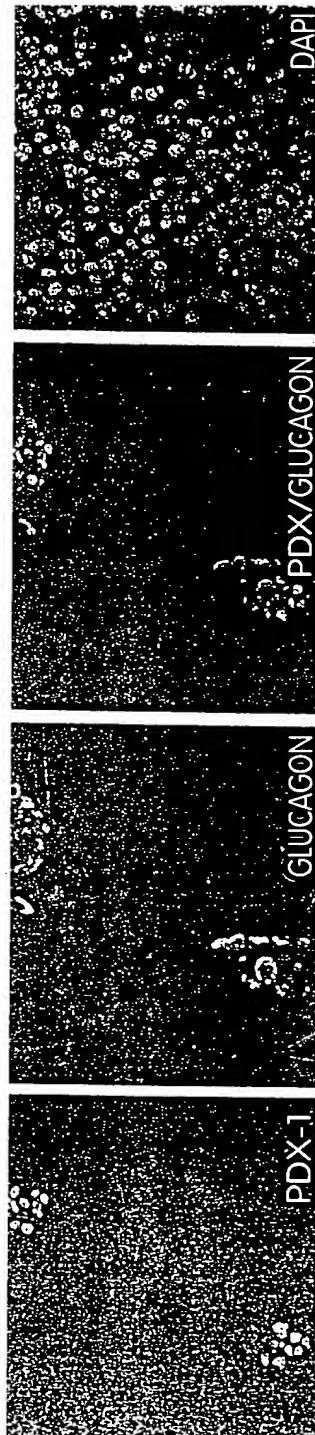
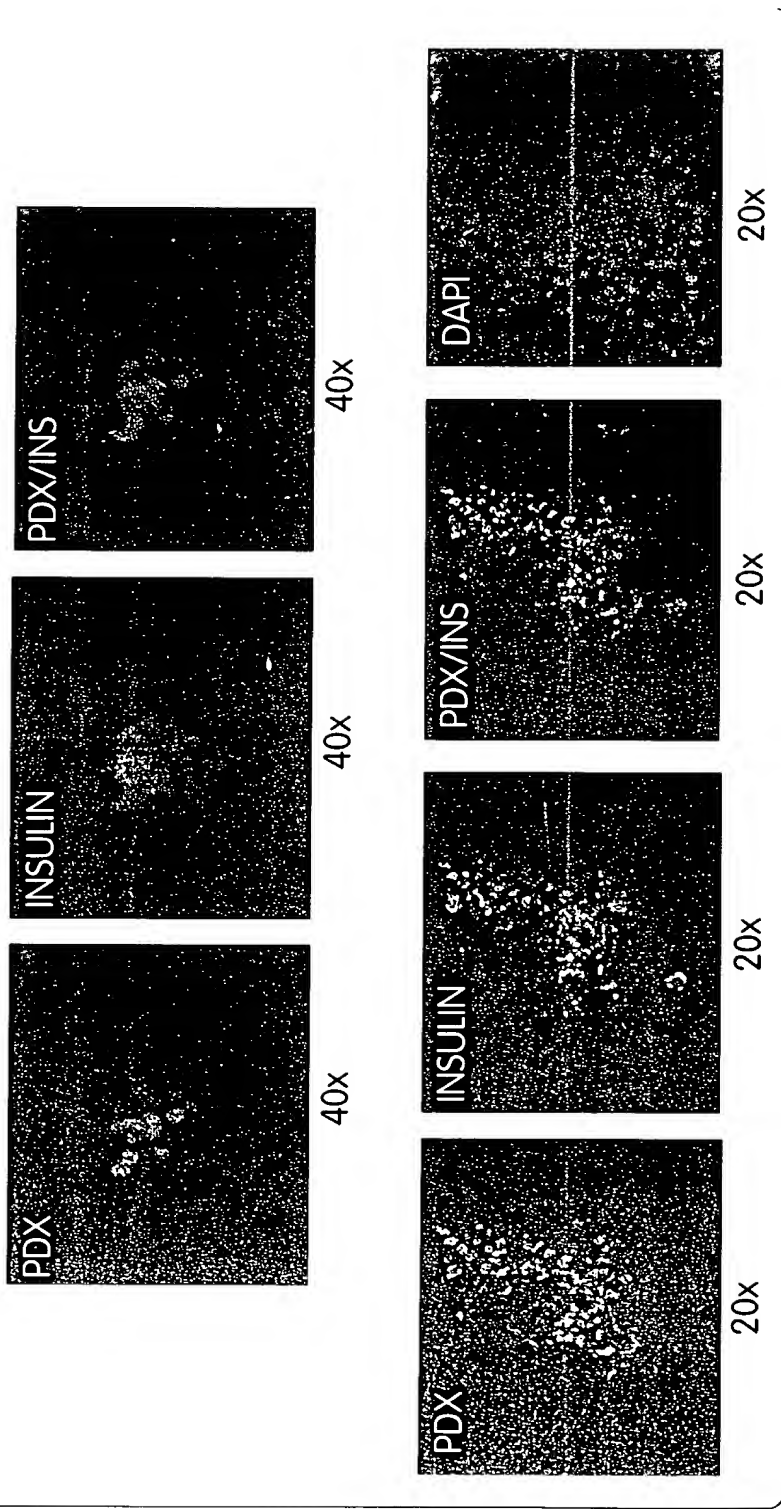


Fig. 44

DUCT SPHERE CELL *IN VITRO* DIFFERENTIATION  
- PDX / INSULIN





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### INSULIN POSITIVE CELLS IN PRIMARY DUCT SPHERES DURING GROWTH AND DIFFERENTIATION IN VITRO

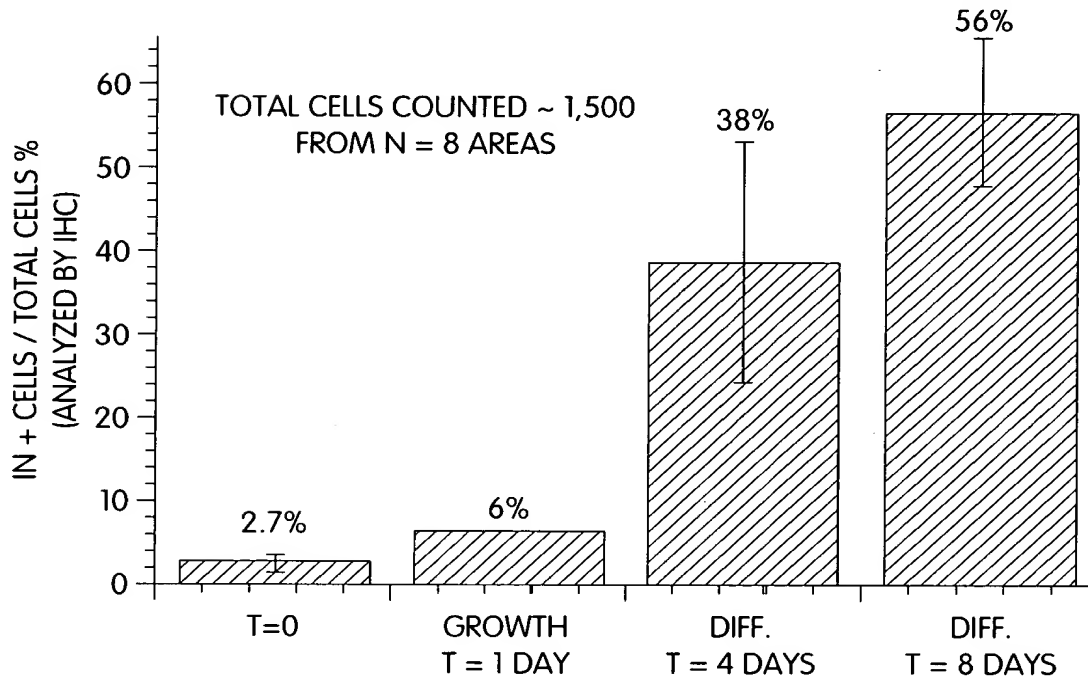


Fig. 46A

### Glut-2 AND IN POSITIVE CELLS IN PRIMARY SPHERE DURING GROWTH & DIFFERENTIATION

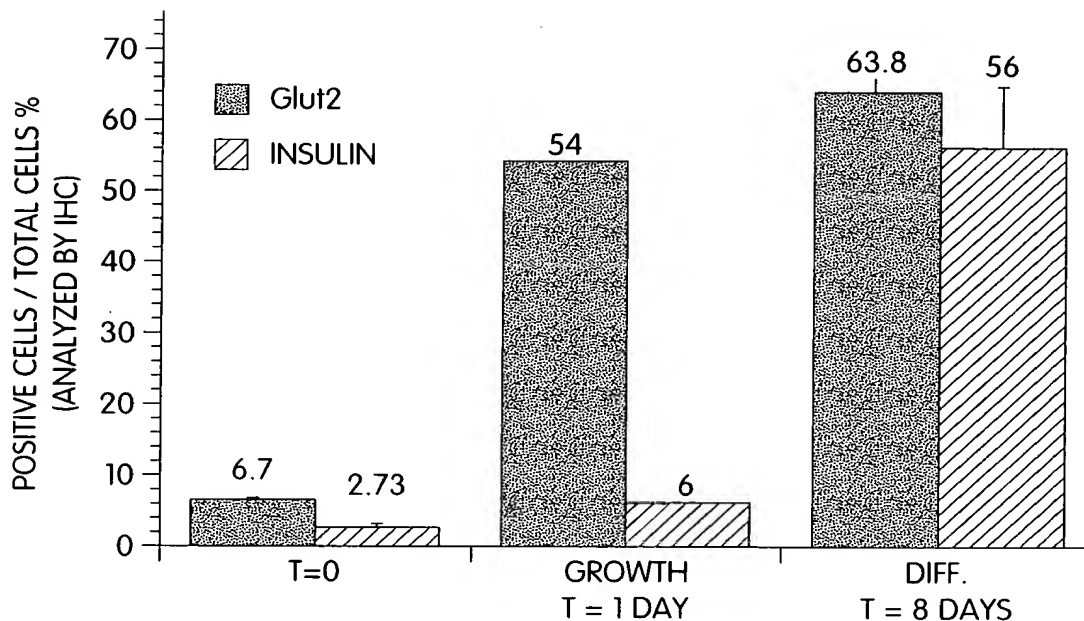
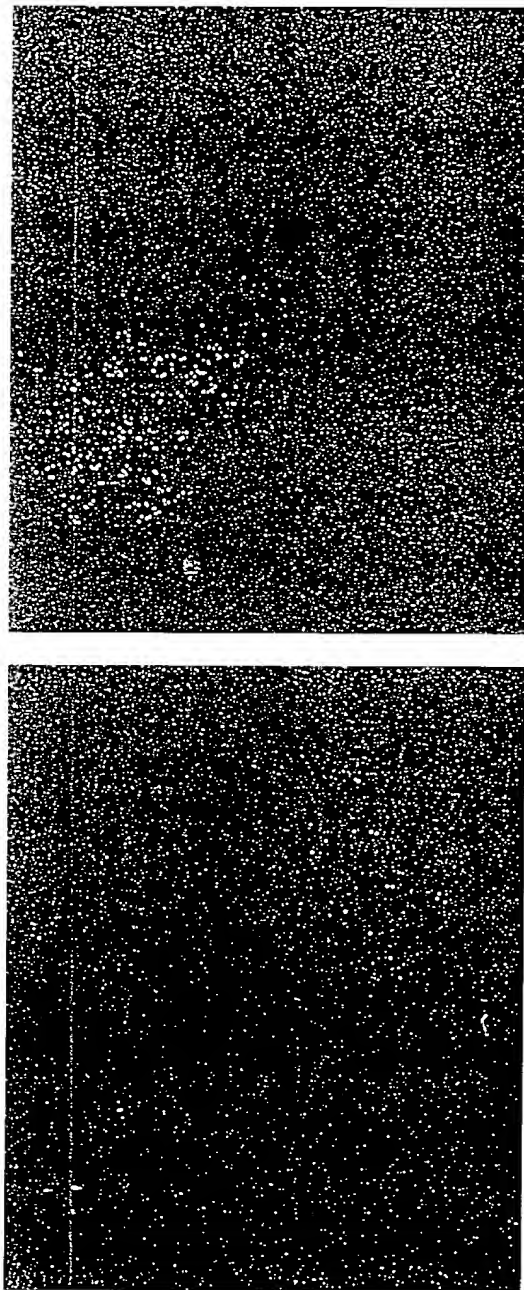


Fig. 46B

5.19 SPHERES ON CYTOSPIN SLIDE  
(SPHERE IN CULTURE FOR 24 DAYS)

NESTIN

DAPI



NESTIN/DAPI

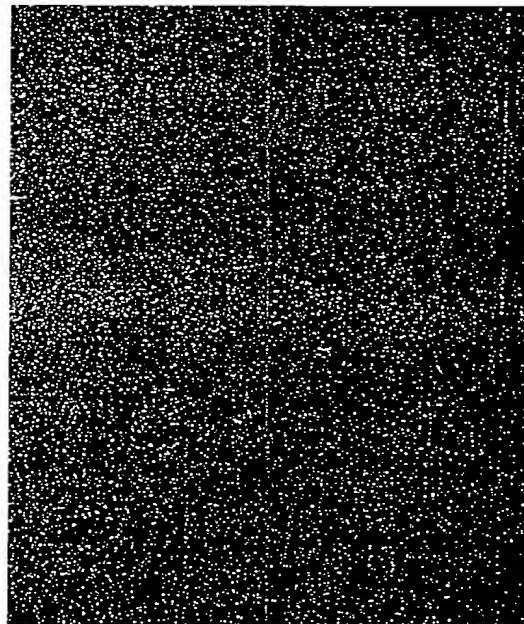


Fig. 47



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TABLE 1: MARKER STAINING IN 5.19-SPHERES ON CYTOSPIN  
SLIDES (UNDIFFERENTIATED CELLS)

(SPHERE IN CULTURE FOR 24 DAYS)

<u>MARKERS</u>	<u>POSITIVE CELLS/TOTAL CELLS</u>	<u>Ave:</u>
Pdx+	20/627 16/520 10/366 3/493	2.2 +/- 0.4%
IN+	10/627 8/520 6/366 3/493	0.11 +/- 0.03%
pdx/IN		60%
glut2+	5/562 6/495 2/503	0.82 +/- 0.03%
Nestin+	314/562 222/495 250/503	52 +/- 3.2%
glut2/nestin		0

Fig. 48



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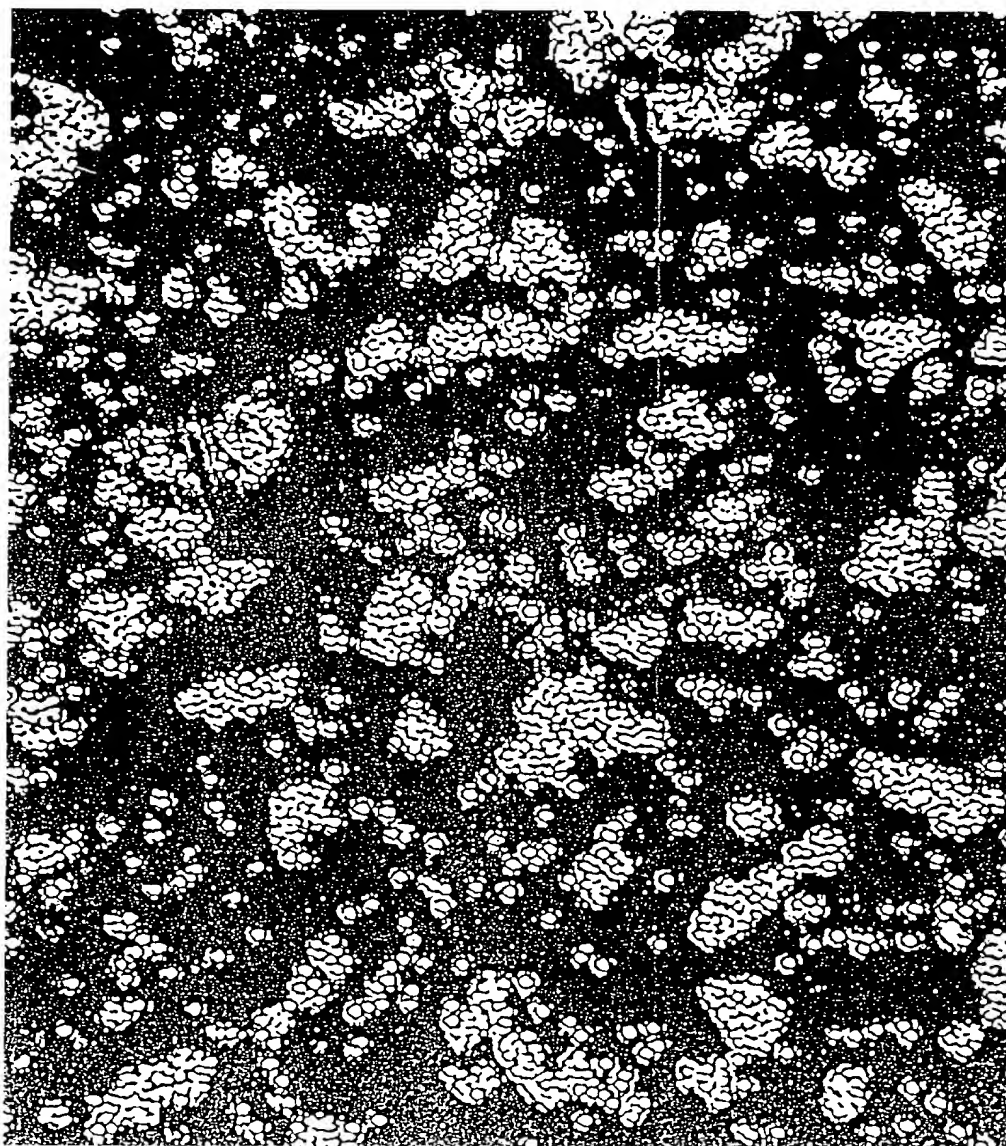


Fig. 49



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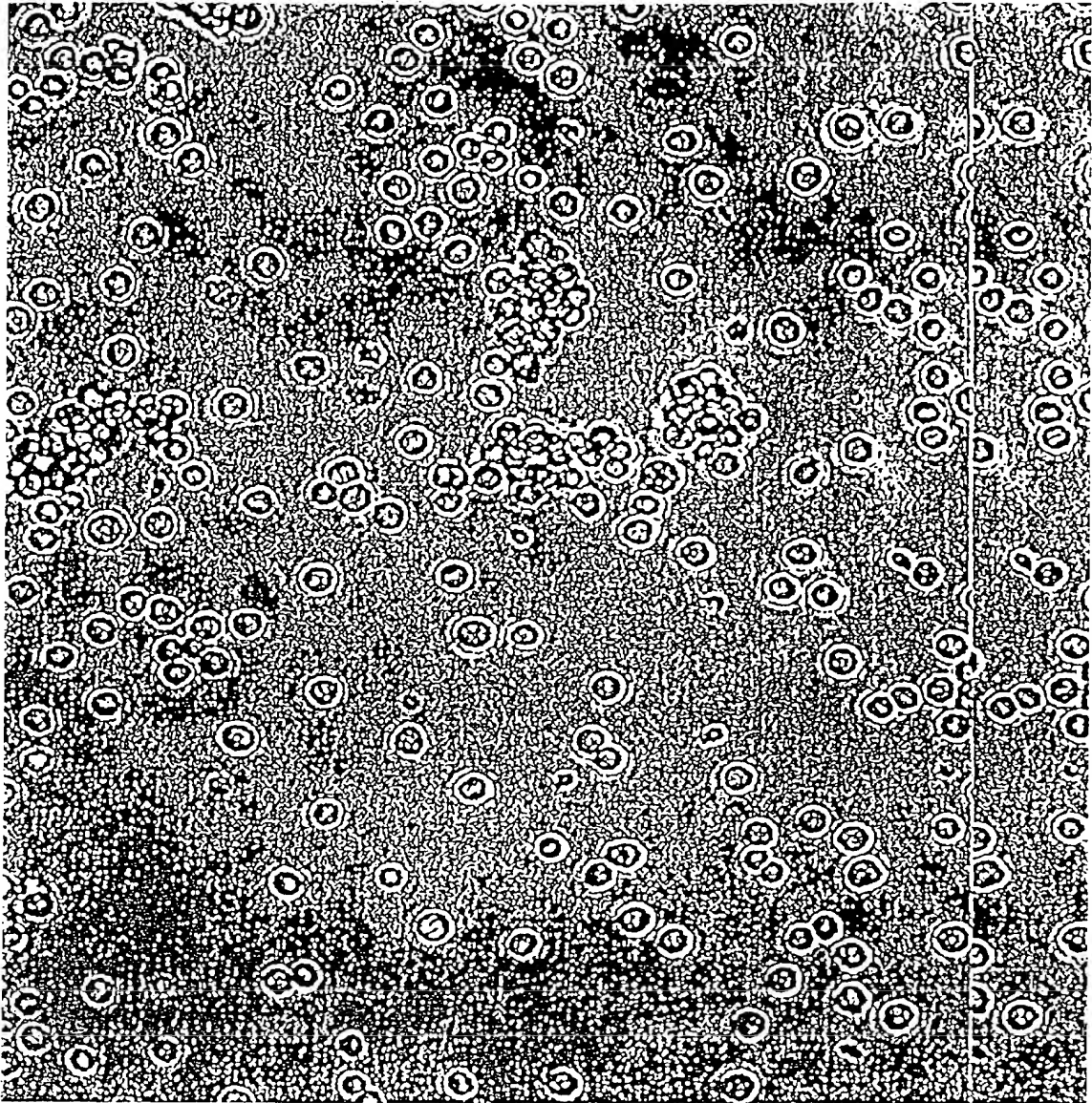


Fig. 50



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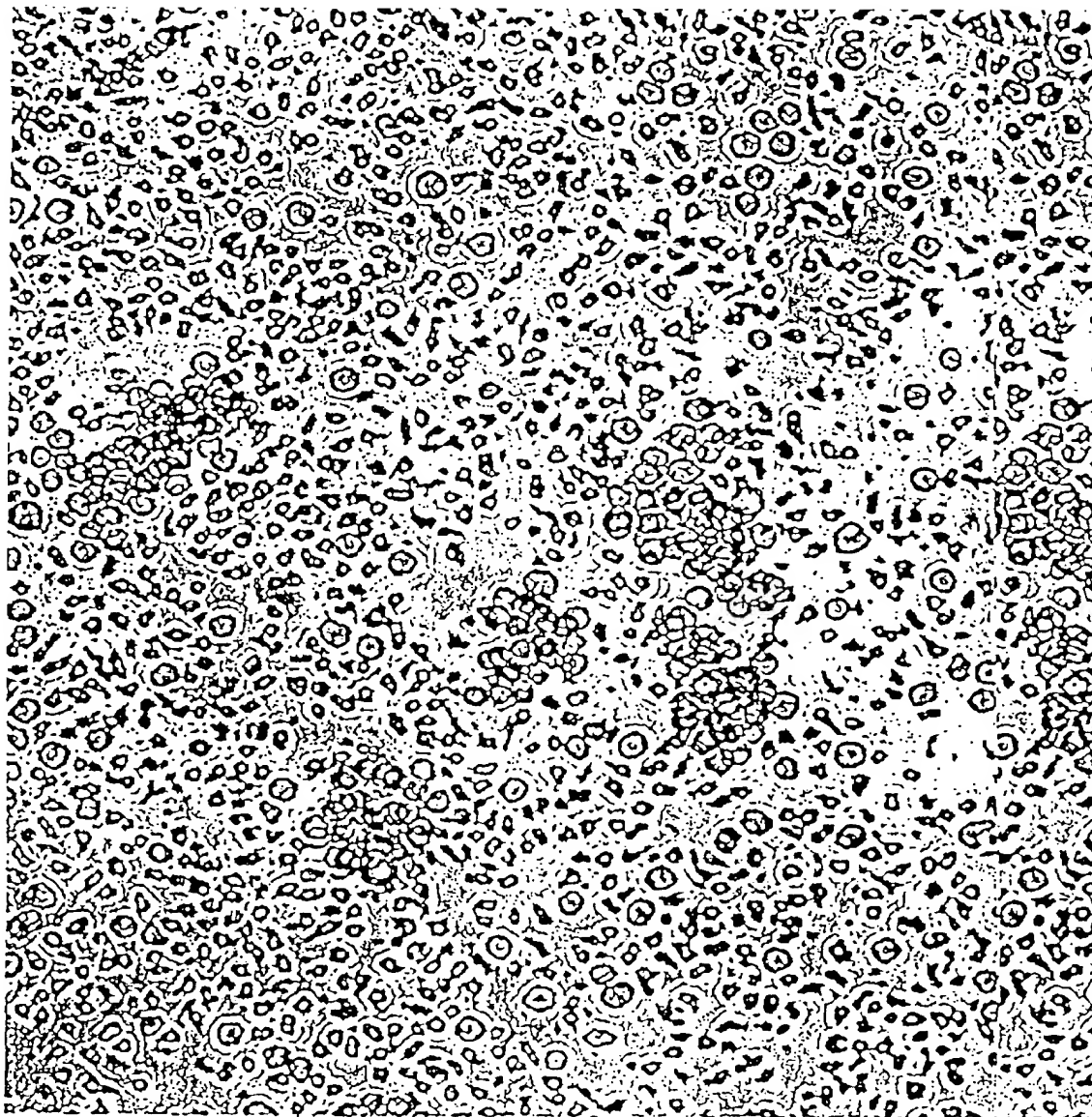


Fig. 51





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### STARTING POPULATION

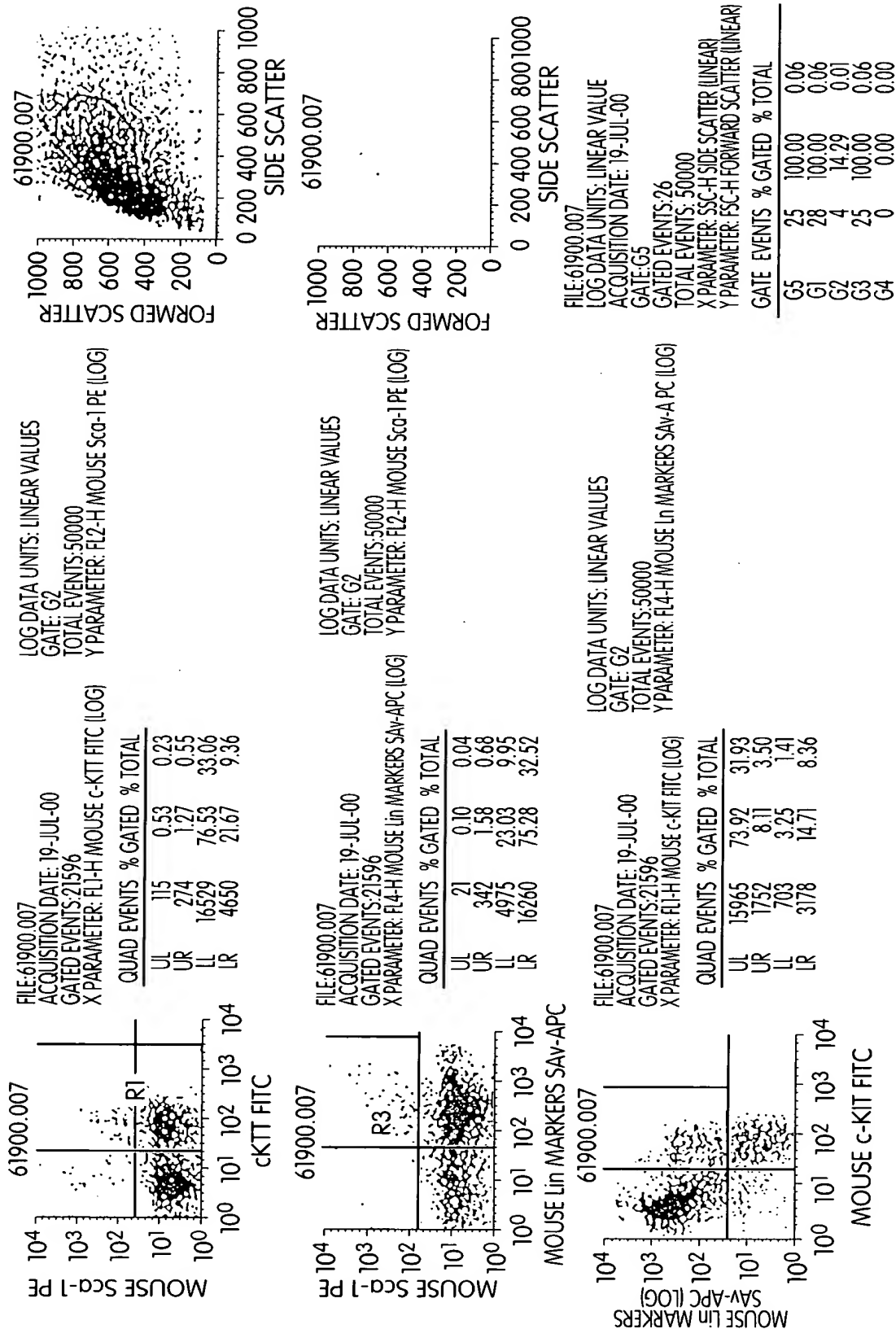


Fig. 52



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### AFTER LINT DEPLETION

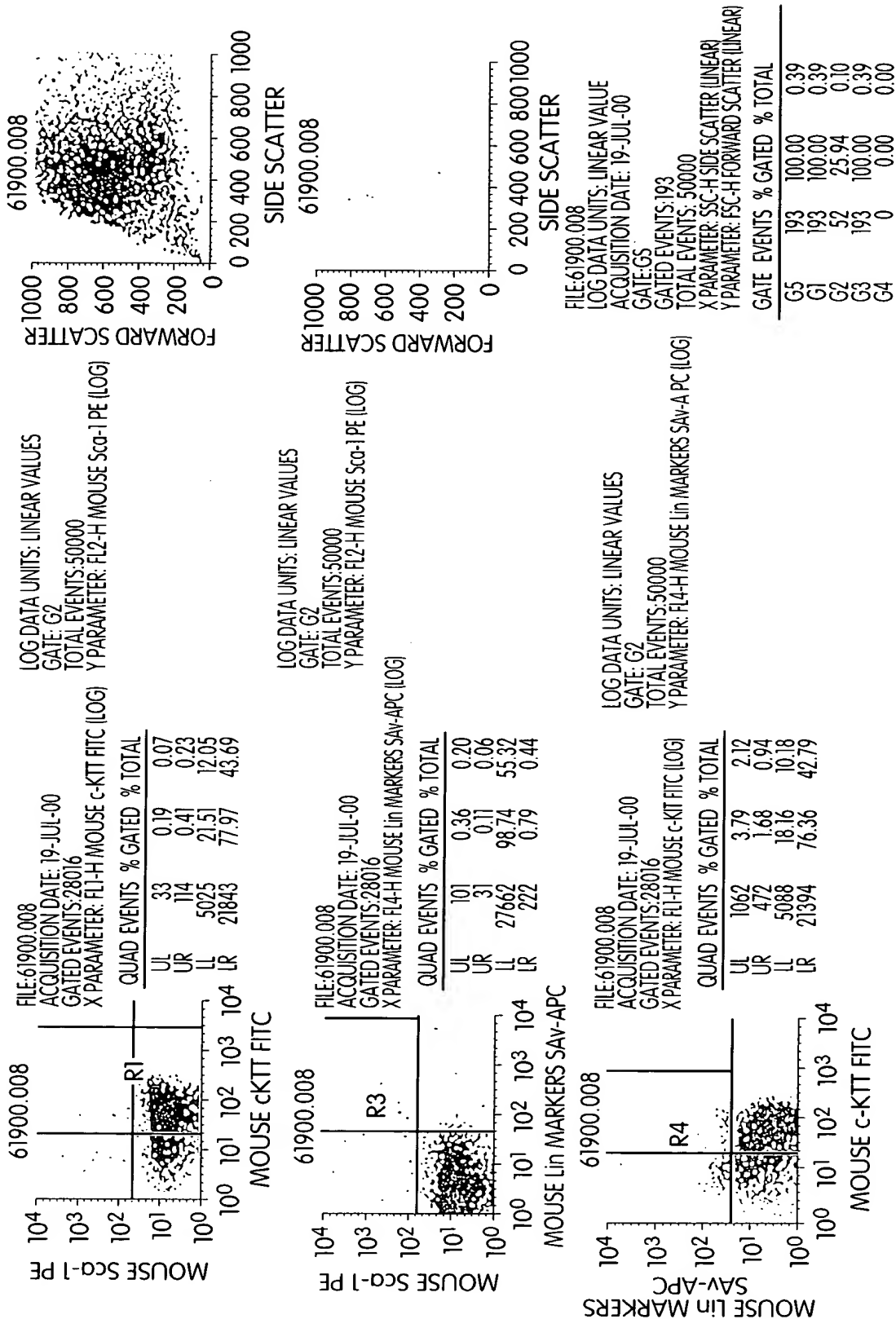


Fig. 53





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### AFTER 20 DAYS IN CULTURE

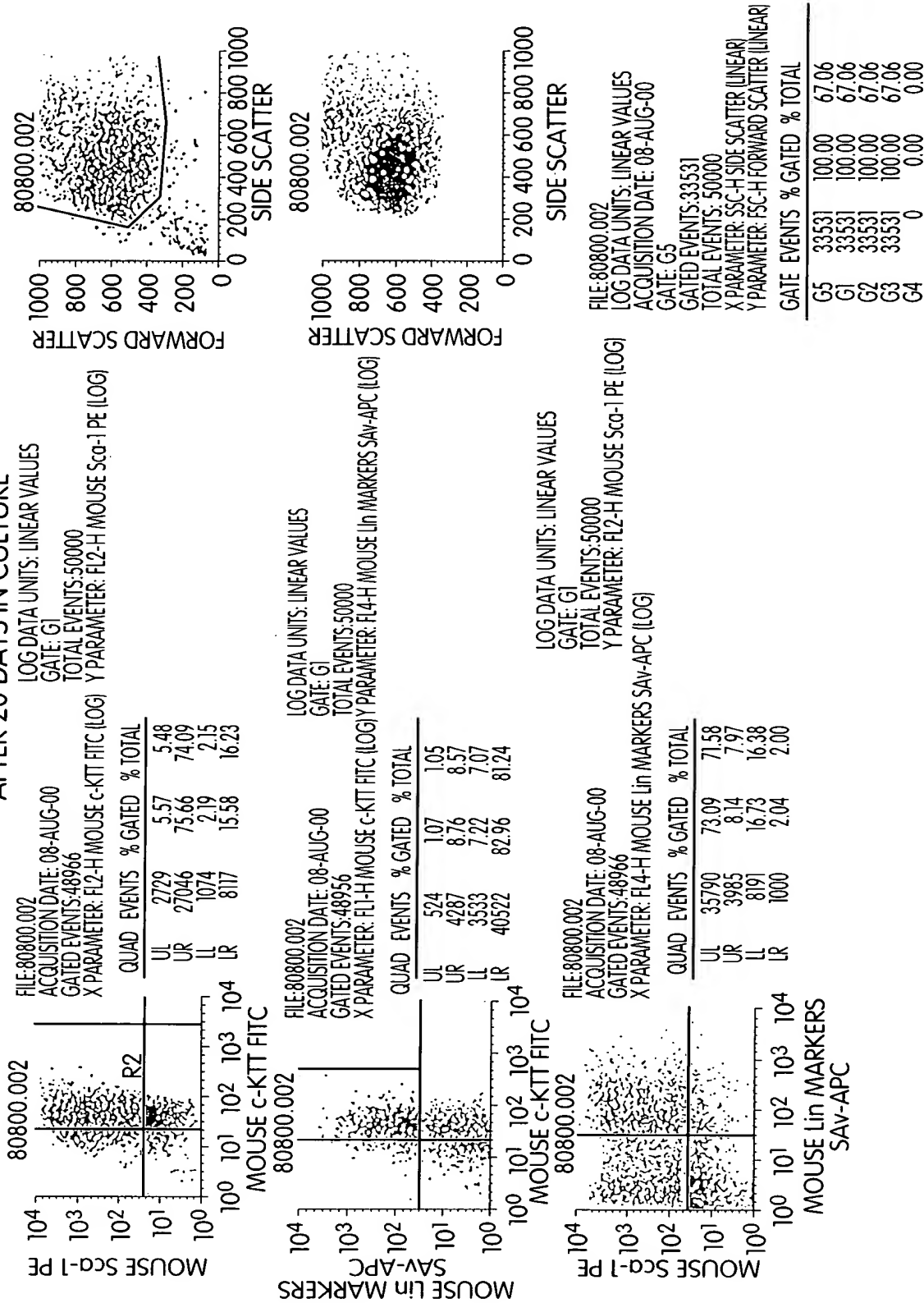
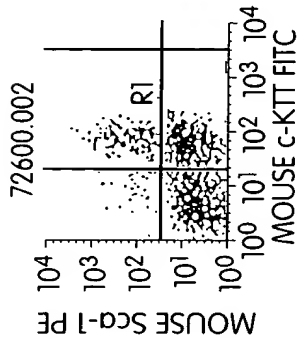


Fig. 55



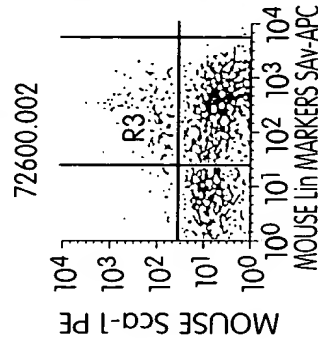
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## STARTING POPULATION



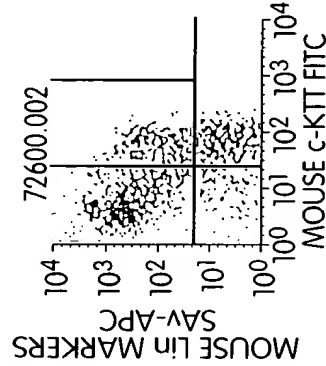
FILE:72600.002  
ACQUISITION DATE: 26-JUL-00  
GATED EVENTS:16726  
X PARAMETER: FL1-H MOUSE c-KIT FITC (LOG)  
LOG DATA UNITS: LINEAR VALUES  
GATE: G2  
TOTAL EVENTS:50000  
Y PARAMETER: FL2-H MOUSE Sca-1 PE (LOG)

QUAD	EVENTS	% GATED	% TOTAL
UL	150	0.05	0.22
UR	1194	7.14	2.39
LL	9406	56.24	18.81
LR	5967	35.67	11.93



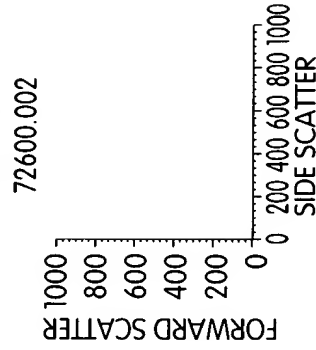
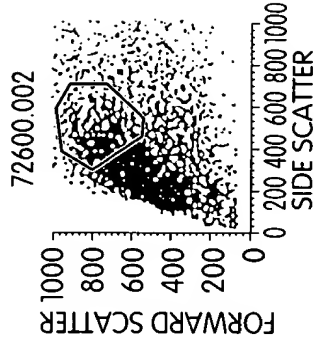
FILE:72600.002  
ACQUISITION DATE: 26-JUL-00  
GATED EVENTS:16726  
X PARAMETER: FL4-H MOUSE Lin MARKERS SAV-APC (LOG)  
LOG DATA UNITS: LINEAR VALUES  
GATE: G2  
TOTAL EVENTS:50000  
Y PARAMETER: FL2-H MOUSE Sca-1 PE (LOG)

QUAD	EVENTS	% GATED	% TOTAL
UL	118	0.71	0.24
UR	1197	7.16	2.39
LL	4899	29.28	9.80
LR	10512	62.85	21.02



FILE:72600.002  
ACQUISITION DATE: 26-JUL-00  
GATED EVENTS:16726  
X PARAMETER: FL1-H MOUSE c-KIT FITC (LOG)  
LOG DATA UNITS: LINEAR VALUES  
GATE: G2  
TOTAL EVENTS:50000  
Y PARAMETER: FL4-H MOUSE Lin MARKERS SAV-APC (LOG)

QUAD	EVENTS	% GATED	% TOTAL
UL	9077	54.27	18.15
UR	2948	17.61	5.89
LL	794	4.75	1.59
LR	3909	23.37	7.82



FILE:72600.002  
LOG DATA UNITS: LINEAR VALUES  
ACQUISITION DATE: 26-JUL-00  
GATE: G5  
GATED EVENTS:135  
TOTAL EVENTS:50000  
X PARAMETER: SSC-H SIDE SCATTER (LINEAR)  
Y PARAMETER: FSC-H FORWARD SCATTER (LINEAR)

GATE	EVENTS	% GATED	% TOTAL
G5	136	100.00	0.27
G1	136	100.00	0.27
G2	63	46.35	0.13
G3	135	100.00	0.27
G4	0	0.00	0.00

Fig. 56



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## AFTER LINT DEPLETION

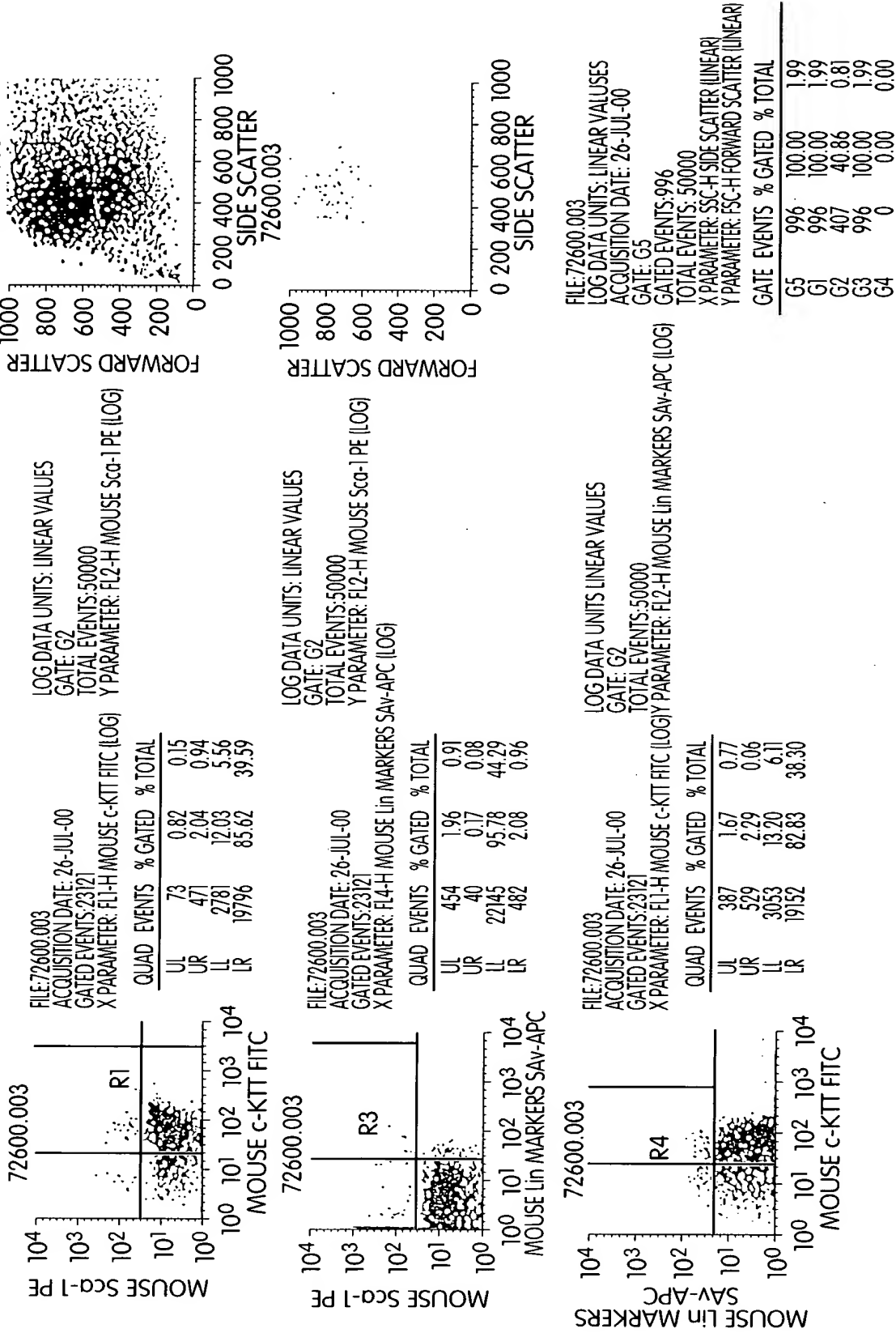


Fig. 57

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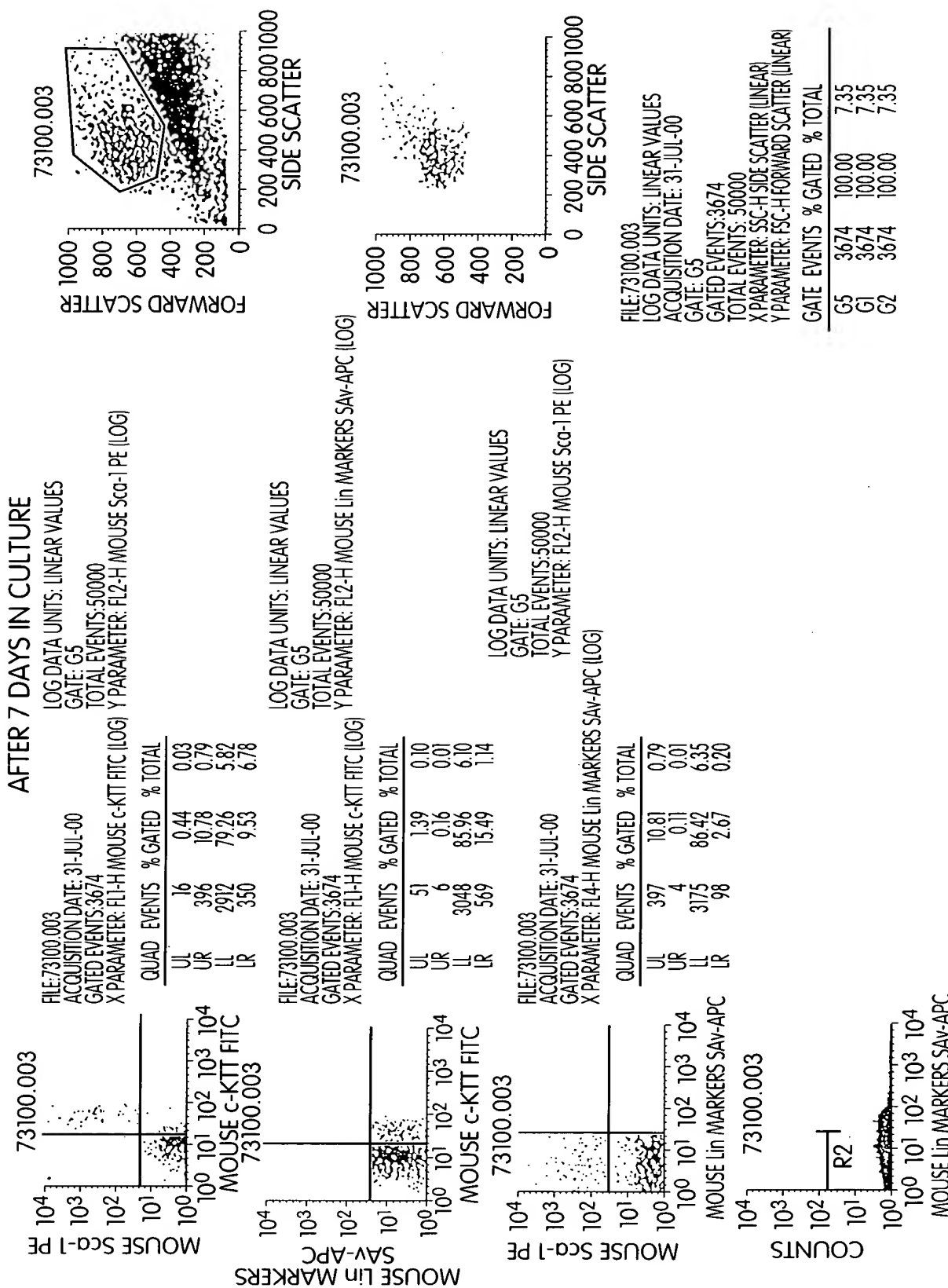


Fig. 58



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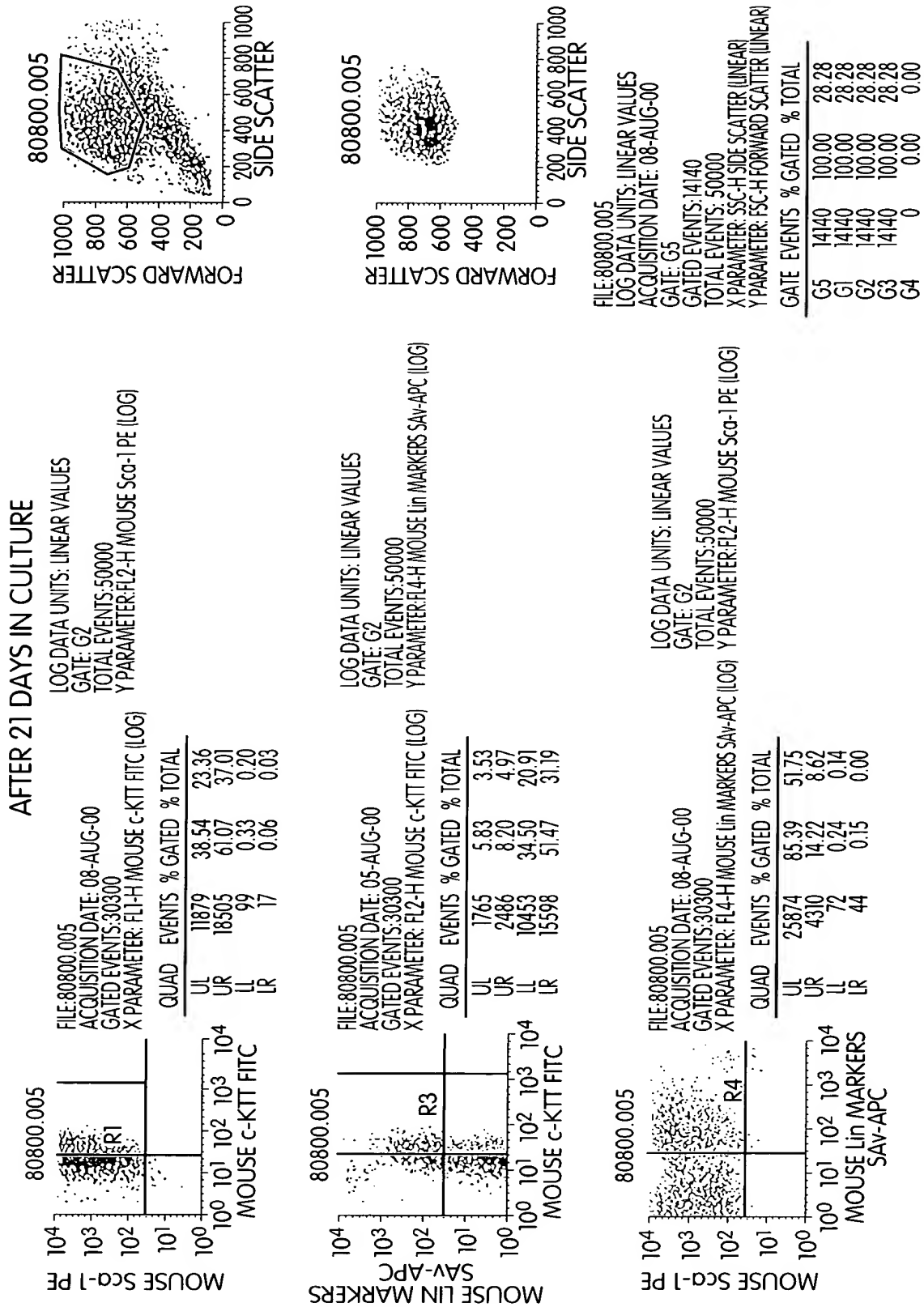


Fig. 59





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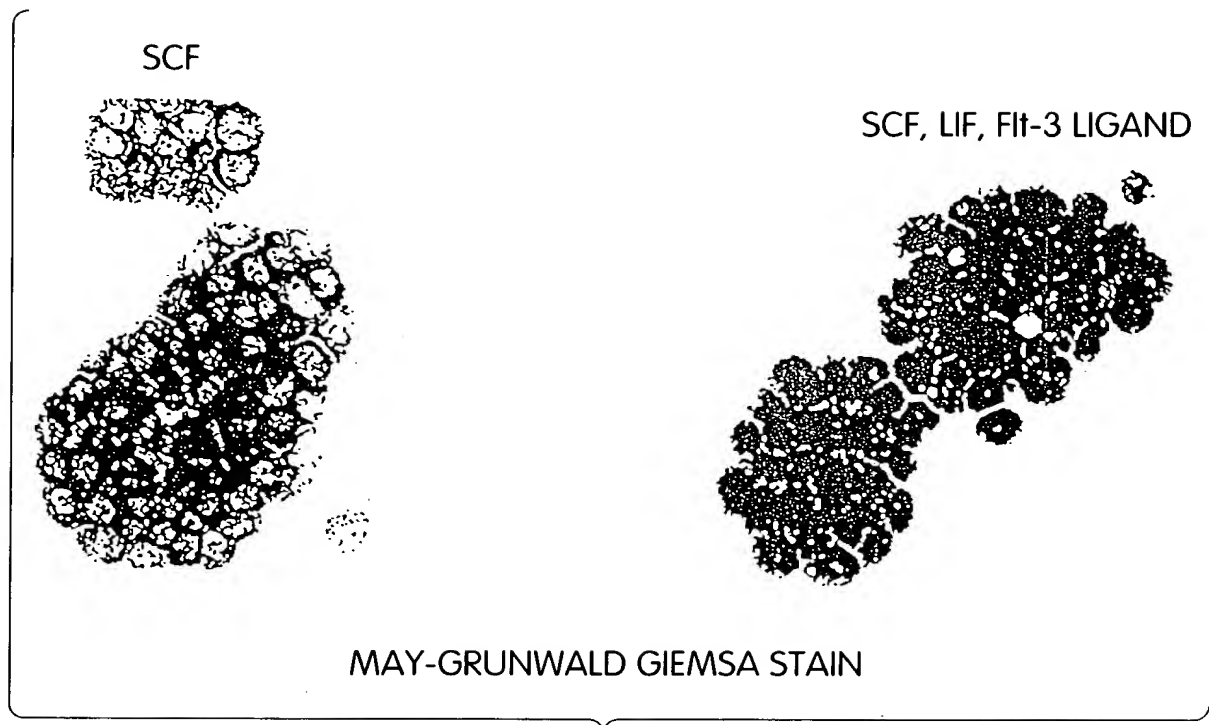


Fig. 60